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The Journal of Laboratory and Clinical Medicine

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ORIGINAL ARTICLES

THE APPLICATION OF THE TYPHOIDIN TEST IN A GROUP OF NURSES AND PHYSICIANS*

BY FREDERICK P. GAY, M.D. (UNIVERSITY OF CALIFORNIA) AND ALBERT R. LAMB, M.D.

THERE seems little reason further to doubt that the skin sensitiveness to preparations of the typhoid bacillus (typhoidin) described by Gay and Force[1] in typhoid vaccinated individuals and in typhoid recoveries is to a large extent specific. Their findings have been essentially confirmed by Pulay,[2] Mehler,[3] Nichols,[4] Kilgore,[5] and Kolmer and Berge.[6] Technical error accounts for the failure of Austrian and Bloomfield[7] to confirm their results.

Question, however, may still exist as to the technic of the test itself and as to the interpretation of the results obtained, and this communication would deal with a separate group of individuals studied from these standpoints. A fuller discussion of all the questions that have arisen in connection with this reaction will appear in a forthcoming article by Force and Stevens[8] with whose work we have been in touch and to whom we are indebted for the improved method applied in this study to a group of one hundred and fifty-four nurses, physicians, and attendants in the Presbyterian Hospital of New York City.

The technic of the typhoidin test as originally described by Gay and Force consisted in the application of a killed, concentrated, old glycerine broth culture of a single strain of B. typhosus to the slightly abraded surface of the arm. A positive reaction differed from a negative result in a quantitative difference in millimeters in the diameter of the areola which appeared around the abraded surface, as read after twenty-four hours. Kilgore[5] has attempted with some success to standardize this technic and eliminate the subjective cause of error by establishing a typhoidin quotient. Another improvement consisted in preventing a recognized deterioration in the fluid typhoidin by precipitating and

*From the Medical Clinic of Columbia University, Presbyterian Hospital, New York.

drying the active constituents by means of absolute alcohol and ether (Gay and Claypole[9]). Of greater significance are the additional modifications introduced by Force and Stevens[8] which are briefly as follows: first, the use of a polyvalent preparation from several chosen strains of typhoid bacilli to allow for the probable varieties and corresponding antigenic differences in typhoid bacilli (Hooker[10]); second, the employment of a carefully determined minimal effective dose of the dried polyvalent typhoidin (0.00002 gm. in 0.05 c.c. of 0.5% carbolated saline); third, the injection of this dose *intradermally;* and, finally, the reading of the reaction in forty-eight instead of twenty-four hours. This later period tends to eliminate the nonspecific irritative reaction which may occur in normal individuals from the proteins of the culture media or the phenol employed as a diluent.

In the adjoining table are summarized the results obtained in vaccinated individuals, typhoid recoveries, and normals by the technic just described. The criterion of a positive reaction consists in the presence after forty-eight hours of a definite indurated papule plus a reddish areola of at least five millimeters. In no instances was a definite papule present without an areola, although the reverse relation was in a few instances the case. No suggestive or doubtful reactions are included, but in any case where doubt existed the test was repeated and any result which did not meet the specified criterion was classed as negative. Repeated tests agree in almost every instance.

SUMMARY OF TYPHOIDIN REACTIONS IN NURSES AND PHYSICIANS AT THE PRESBYTERIAN HOSPITAL.

	No. Examined	Positive	Negative	Per Cent Positive
I. Cases giving a definite history of antecedent typhoid fever (2 to 22 yrs. previously)	12	9	3	75%
II. Vaccinated cases.				
Within six months (New York Board of Health Vaccine)	29	19	10	65.5%
Six months to 1 year "	50	32	18	64%
One year to 18 months. P. H. vaccine	24	18	6	75%
Two years to 30 months. " "	13	7	6	53.8%
Three to five years. Various vaccines.	5	2	3	40%
III. Normals giving no history of typhoid or typhoid vaccination.	21	3	18	14.28%

Great pains were taken to obtain a careful history in those cases listed as typhoid recoveries, and they may be accepted as fully as accurate as most histories of this sort, although in the majority of cases no certain history of blood cultures and Widals was obtained. On the other hand, in the normals (Group III) care was taken to exclude those with history of any continued fever. There were five individual cases in which the history of previous typhoid was suggestive with two negative and three positive typhoidin tests which are not included in the table.

It will be noted that the majority of the vaccinated cases had been immunized with vaccines supplied by the New York Board of Health, or else prepared in the Bacteriological Laboratory of the Presbyterian Hospital. The Board of Health vaccine, was, we understand, prepared from the well-known

army or Rawling's strain.[11] The Presbyterian Hospital vaccine was prepared from a strain of B. typhosus grown there on artificial media for some twenty years, and originally isolated from the spleen at autopsy. In all these instances the dosage and intervals were the same, namely, three doses of five hundred thousand, one million, and one million bacteria, at weekly intervals.

A survey of the percentage of positive results shows that seventy-five per cent of those individuals that had recovered from typhoid gave a positive reaction. The negative reactions bear no relation to the date of the antecedent disease since two cases twenty-two years previously were both positive. From seventy-five to forty per cent of those that had been vaccinated against typhoid also reacted positively and in general in decreasing correspondence with the lapse of time since immunization. The higher percentage with the Presbyterian Hospital vaccine in the group between one year and eighteen months previously may be accidental or may point to a fresher or more antigenic vaccine.

The results obtained in this group of cases correspond very closely to those recently obtained by Force and Stevens.[8] The percentage of typhoid recoveries giving a positive reaction is not, however, so high as in the original communication of Gay and Force,[1] which may depend on a more rigorous criterion of determination, or possibly may be a more correct indication of the degree of protection which is actually afforded by recovery from typhoid fever. It has generally been assumed that recovery from this disease protects in the great majority of cases, and in statistics over long periods of time it has been found by most observers (Curschman,[12] McCrae[13]) that only two or three per cent of cases of typhoid fever give a previous history of the disease. Such figures would seem an overestimate rather than an underestimate, since the period at which these figures were obtained antedated the differentiation between typhoid and paratyphoid, which must have been confused. On the other hand, more recent investigations by Sawyer [14] and Kelly [15] show that under conditions of massive infection from eight to fifteen per cent of the cases of typhoid may give histories of previous typhoid fever. Protection against typhoid, either by recovery or by vaccination must in all cases be regarded as relative, and it is probable that any recovered case of typhoid fever could be infected with the disease if a sufficient dose of living typhoid bacilli were ingested.

The percentage of presumably normal individuals (14.28%) that give a positive typhoidin reaction corresponds closely to the nine per cent originally described by Gay and Force,[1] and the eleven per cent of Gay and Claypole.[9] Such cases are extremely interesting, and the question at once arises as to whether they are individuals with some peculiar nonspecific susceptibility of the skin, or as to whether they may at some time have undergone an unsuspected infection with B. typhosus. An apparently well-controlled instance of abortive attacks of typhoid fever in a group which also showed unmistakable, well-defined instances of the disease, all of which gave positive typhoidin tests, has already been referred to by Gay and Claypole.[9] Another possibility is that certain of these normals who react as do typhoid recoveries may be healthy carriers of B. typhosus. An attempt to verify this latter hypothesis has recently been made

on two students of the University of California, who gave absolutely no history of typhoid fever and who had not been vaccinated protectively. Both gave a clear-cut, positive reaction to typhoidin. The Widal in both cases was negative in a dilution of 1-10, and an attempt to isolate the typhoid bacillus from the urine and from the stools after elaterin catharsis[16] was negative.

Repetition should be made of the purpose for which this test is employed, as compared with any interpretation of what its true significance may be. Since the reaction occurs in those individuals who are known to be more or less perfectly protected against typhoid fever, the test was originally offered as presumptive evidence of protection in the individual case when positive. We have seen no reason to alter our opinion in this respect, and would point out further indications that this interpretation of the reaction is true, in addition to the simple relationship observed. In the first place, in no individual, in whom a positive reaction has been obtained, has typhoid fever occurred. This might well be due to the relatively small number of such observations that have been made, but it is interesting to find that, on the other hand, in three individuals, who have been vaccinated and in whom a negative reaction was subsequently obtained, typhoid fever shortly thereafter occurred. Two of these individuals were laboratory workers and exposed, and indeed known in one instance to have been subjected to massive infection; the other was a nurse who attended a typhoid patient. In the second place, individuals who react positively, when re-inoculated with typhoid vaccine react much more violently than do individuals who give a negative typhoidin test, in this respect resembling typhoid recoveries, and certainly indicating a reaction and probably protection against B. typhosus. And, finally, individuals who have been vaccinated against typhoid and who react negatively become positive in most instances on further immunization. We regard the attempt of Nichols[4] to explain the typhoidin test as an indication of hypersusceptibility rather than of true immunity as supererogatory in view of the fact that both conditions would seem to be coincident.

At all events, whatever may be the eventual understanding of a positive typhoidin test, use of its absence as an indication for re-vaccination certainly errs on the side of safety in detecting those individuals who in spite of typhoid vaccination do not show indications of a reaction to the typhoid bacillus, and who are, therefore, presumptively those particular individuals who under ordinary conditions of infection will be found to be the least protected ones.

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CARDIAC ANEURISMS*

By Paul G. Woolley, M.D., Cincinnati, Ohio.

CARDIAC aneurism is a subject I have chosen because the condition is relatively uncommon, and rarity introduces a certain modicum of interest that one may not feel in a discussion of the plain ordinary aneurisms which are more frequently seen. It illustrates the whole subject of aneurism so that in speaking of it one may apply the principles involved in vascular aneurisms, and therefore the interest in the less common condition may be carried to the more usual one.

The heart is after all merely one section of the vascular tree in which arrangements have been made for a certain temporary storage of blood, and in which the mechanism for propulsion of the blood has been developed. Accordingly the possibilities of dilatation have been increased and the contractile tissue of the walls has been augmented to meet the physical demand of forcing a large volume of blood against a constant pressure. Moreover, in order that the blood flow shall prevail in but one direction, the valves, which are endocardial reduplications, and which correspond to the valves of the veins, are highly developed. Structurally, therefore, the heart and the aorta, in which aneurisms are most frequently seen, (not to speak of the other parts of the vascular system) differ from one another merely in the amount of muscle on the one hand, and elastic tissue, on the other. The physiologic activity of the heart, therefore, depends largely upon the quality and quantity of the myocardium, while that of the aorta depends largely upon the quality and quantity of the elastic tissue. The quality of any tissue depends upon the amount of nourishment it receives; which means, as a rule, the amount of normal blood supplying it. The amount of blood arriving at any point of a tissue depends upon the pressure, within or upon, the organ, and upon the condition of the smaller vessels carrying the blood. In ileus, the muscular wall of the gut becomes paralyzed largely because the dilatation (the internal pressure) cuts down the blood supply. In decubitus the skin sloughs

*From the Pathologic Institute of the Cincinnati General Hospital and the Mary M. Emery Department of Pathology of the University of Cincinnati. Read at a meeting of the Pathologic Section of the Lucas County Academy of Medicine, Dec. 8, 1916.

because external pressure cuts off the blood supply. Degeneration and necrosis take place in acute inflammatory foci because the tissues between the smaller vessels swell and compress the vessels, or, in more chronic cases, because overgrowth of fibrous tissue takes place; and this, in its development and later contraction, compresses the vessels.

In the heart the course of events is roughly as follows: The infecting organisms—in syphilis, the spirochetes—arrive by way of the blood stream and enter the smaller vessels of the myocardium from which they pass into the perivascular spaces. Here they set up an inflammatory change of a chronic order which is characterized by accumulations of small round cells, and a slight edema of the connective tissue cells and of the myocardium. The sequel of this small celled infiltration is perivascular fibrosis which is associated with a minimum of myocardial degeneration. As time goes on two things happen. First, the perivascular connective tissue becomes well-formed and contracts, limiting the flow of blood through the vessels; and second, it becomes, because of its increased thickness and concentrated colloidal character, less permeable to the dissolved food stuffs of the blood. The result is that the food supply of the myocardium is gradually diminished and atrophy occurs. Then, because of the relative lack of contractile tissue, strain is placed upon the remaining fibrous tissue which is apt to undergo hypertrophy, and so fibrosis appears. Each area of fibrosis represents a point of weakness,—a point at which the wall of the heart is less resistant to continued pressure. In the aorta the same process commences about the vasa vasorum and it is this that accounts for the characteristic pearly, succulent, raised patches, and for the intimal puckerings. Sections through these pearly patches show an intact endothelium, a hyperplastic subintimal connective tissue, (the result of strain, I take it), an atrophied muscularis, and a degenerated disappearing elastica, and about the vasa, which supply the outer two-thirds of the vascular wall, well marked small round cell infiltration. From this time on the changes are degenerative. These terminal degenerative changes are the ones which produce the appearances which are indistinguishable from those associated with the ordinary ones of the so-called senile atherosclerosis. They are developed because of interference with the nutrition of the scar tissue in exactly the same manner as the primary degeneration of the media. The course of events is as follows: The normal aortic wall is nourished in its outer two-thirds by a direct vascular supply. The inner third receives its nourishment by indirect means, from the lumen by absorption and from the outer vascular layers also by absorption. Therefore, when medial and subintimal fibrosis has developed to a certain degree, and especially when the blood supply to the outer two-thirds has been reduced as we have described, a relative lack of "food' is developed and the newly formed tissue tends to die, in evidence of which, what one knows as lipoid and fatty degeneration occurs, and atheromatous abscesses appear, which, as time goes on, either become ulcers, or, becoming calcified, form placques.

There are two periods during which the vessel wall or the myocardium, as the case may be, is particularly weak; i. e., during the period of more acute inflammatory change, and during the period of degeneration. At either period an aneurism may develop provided the physical conditions (i. e., internal pres-

sure) are propitious. Usually, during the latter stage which appears relatively late, the individual is less active and the internal pressure is relatively low. Aneurisms are, therefore, less frequent in old age. On the other hand, during the early stages, the individual is active, and apt to be subjected to physical strain.

This factor of strain, while it seems to be a secondary factor in the production of aneurisms, also seems to be a necessary one. The primrose path by itself does not conduce, of itself, to aneurism, but as a person follows it, it seems that he must stop occasionally and do some hard work if he is to have an aneurism. This is why it is the young men, men from 30 to 45, who are the sufferers from this condition. In my series of 24 aortic aneurisms, 14 were in patients under 50 years of age; 20, under 60 years. In a series of 12 diffuse aortic dilatations, 10 were under 60 years of age. In a series of eight perforating aneurisms one was 27 years old; one, 35; two, 37; one, 40; one, 42; and two, 43. In the present series of cardiac aneurisms, one was 35 years of age, the other four were in the early fifties. In these series, if one makes allowance for the time during which the lesion has been developing, one sees very clearly that aneurism is a disease of years preceding middle age, the time of greatest physical activity.

These are briefly the facts of arteriosclerosis. They have been applied less generally to the heart. Nevertheless they do apply to the heart fully as well as to the vascular system. Let us summarize them as follows: Just as long as the blood supply remains adequate a tissue will do its work within physiologic limits, even if the demands are very great. A heart will hypertrophy just as long as its blood supply (through the coronaries) is sufficient. It will dilate as soon as the blood supply is not adequate. A hypertrophic heart is one which is a well heart; a dilated heart is a sick one. It frequently happens, of course, that the parenchyma of an organ is not able to make use of an available food supply. When this happens it is because the composition of the blood, aside from the nutritive constituents, is abnormal and this reacts upon the muscle to damage it. The abnormal materials in the blood are sometimes soluble and diffused substances (like toxins, phenol, etc.), and then the effects upon the organ are diffuse ones: they may also be discrete, and insoluble (emboli, bacteria, etc.) and then the effects are focal.

So much by way of an introduction.

* * * * *

Cardiac aneurisms bear somewhat the same relation to diffuse cardiac dilatations that vascular aneurisms bear to vascular dilatations. These vascular lesions are most prominent in the aorta, which, if it be affected focally, becomes the seat of local dilatations (aneurisms) and if diffusely damaged, becomes dilated. If a heart is diffusely damaged it dilates as a whole; if focally damaged, it develops a focal dilatation.

Cardiac aneurisms may be acute or chronic. In the acute cases, the dilatation is rapid and definite and depends upon the appearance of areas of softening in the myocardium which are the result of degenerative processes caused by sudden cutting down of the supply of nutriment to the myocardium with or without the presence of bacteria. These sudden vascular effects are the results

of the appearance of thrombi or emboli in the branches of the coronary vessels. Emboli may come from infected valves or from primary seats of disease in other parts of the body. When such sudden degeneration or necrosis (infarction) of the myocardium appears, the cardiac wall is weakened and bulges under the influence of the intracardiac pressure, and, in case the bulging is sufficient, the myocardium ruptures, and hemorrhage into the pericardium occurs. In some cases, because of limitation of the dilatation by pericardial adhesions, rupture does not take place, and if time and infection permit life to persist, the bulging becomes permanent.

On the other hand, well-formed chronic aneurisms result as a rule from focal myocardial fibrosis, caused by chronic coronary circulatory defects, or chronic myocardial infections.

Myocardial fibrosis occurs as a diffuse, or as a focal, process. In the first case it is most frequently, perhaps, a sequel of myocardial overwork, as, for instance, in persons in whom there exists peripheral vascular sclerosis and high blood pressure. It also occurs as a somewhat diffuse process but with a tendency to focal arrangement as a result of certain infections, as, for instance, syphilis, and acute rheumatic fever. It is possible that it is a sequel of other infections which run a subacute course and which are septicemic in character. In the second case it follows the focal myocardial infections, or localized degenerations, such as those which occur as a result of coronary sclerosis.

Chronic cardiac aneurisms result from focal myocardial fibrosis because at the seat of a myocardial scar the heart wall is weakened, not so much because fibrous tissue is weaker than muscle, which it is not, but because it has no "come back"—it is not contractile as muscle is—and so, being stretched by the force of the blood pressure, it tends to remain stretched, and, in the course of time, to be more stretched until it forms a saccular continuation of the cardiac chamber. These aneurisms have a predilection for the anterior wall of the left ventricle, near the apex, a region supplied by the anterior or descending branch of the left coronary, the vessel which supplies the anterior papillary muscle of the left ventricle and the interventricular septum. Since acute complete closure of the artery leads to sudden death of the myocardium, it is apparent that for the production of a fibrosis, the vessel must be gradually changed, as by a developing sclerosis; or the myocardium may be scarred in the course of healing of an acute lesion caused by a small infected embolus which does not block enough of the main vessel to bring about an immediately fatal result.

After the formation of a myocardial aneurism has begun, adhesions between the heart and the pericardium may occur, and the dilatation may be hindered, or, what happens less frequently, the heart may rupture into the pericardium. If there are few or no pericardial adhesions and rupture occurs, death may ensue rapidly; if there are many adhesions, death may be postponed or may occur from some other cause. Also, as in other aneurisms, the sac may become filled with thrombi and prevent rupture, and also the endocardium may become tremendously hypertrophied (fibrosis) and so prevent rupture. "Weeping," or oozing of blood through the wall is not, however, prevented in such cases. Many of the cases of spontaneous rupture of the heart are in reality cases in which the break has occurred in the wall of a cardiac aneurism.

The following cases illustrate the subject of cardiac aneurism:

CASE I.

M. P., No. A-2775, a woman of middle age, was brought to the hospital on May 20, 1916. When she arrived in the receiving ward she was moribund, and died 10 minutes later. No history was obtained.

AUTOPSY PROTOCOL.—The body was that of a short, thick woman, well formed and well nourished. Rigor mortis was not present; postmortem lividity was present. The whole body, above the waist, was covered with scratch marks and in the axilla and the hair of the head there were tremendous numbers of pediculi and ova. Pediculi were crawling on the surface of the body. When

Fig. 1.—Case A-2775. (Case I.) Note the hypertrophied ventricular wall in which the fibrosis is apparent. Especially note the sclerotic endocardium which lines the bulging area. Observe also the thinness of the apical myocardium where the musculature is not bulged showing that even a thin healthy wall may be as efficient as a thick fibrotic one.

the calvarium was removed, there was a gush of thin clear serous fluid in very large amounts. The dura was more than usually adherent to the calvarium and was edematous. The pia was tremendously edematous so that it stood up in large blebs which measured 4 cm. in diameter. Here and there, particularly over the anterior half of the cerebral lobes, the pia was scarred and clouded with fibrosis. There was no evidence of infection. The pia was also decidedly congested. The branches of the Circle of Willis, particularly the basillar, the vertebral and carotids, as well as the smaller branches, showed an exceedingly well-marked condition of arteriosclerosis with calcification. There was no distinct evidence of thrombosis. The dura of the base was generally, but not con-

siderably, thickened and more than normally adherent. There was no evidence of trauma about the head. The peripheral lymph glands were somewhat enlarged and shotty. There were no masses in the breasts. There was a slight edema of the ankles. The finger nails were cyanotic. The pupils were slightly dilated, the right being a little larger than the left. The teeth that remained were in a horrible condition and were represented merely by necrotic, movable stumps. Many of the teeth were almost completely gone superficially and their places were indicated merely by stumps.

The subcutaneous fat was very well developed. The muscles were scantily developed but of good color. The intestines seemed to occupy a normal position; the appendix was *in situ* and evidently healthy. The omentum was coiled up above the transverse colon. There were no adhesions in the pelvis; the tubes and ovaries were free. There was a tremendous congestion of the veins in the ovarian plexus. The lower border of the liver was 9 cm. below the ensiform and 6 cm. below the costal margin in the right mammillary line.

In the pericardial cavity was a slight increase of fluid which was blood-stained—about 25 c.c. There were posterolateral adhesions in the left pleural cavity and a small increase of blood-stained fluid. In the right pleural cavity there were no adhesions.

There were numerous intestinal diverticula about four feet above the cecum. There were old adhesions between the gall bladder and duodenum and between the edge of the left lobe of the liver and stomach.

The spleen was enlarged and quite firm. The capsule was only slightly and generally thickened. On section, the organ was very evidently congested and firm. The Malpighian bodies were visible.

The left adrenal was beginning to show cavitation. The right adrenal showed nothing unusual. The left kidney was somewhat smaller than usual and quite firm; the capsule stripped with comparative ease but left a generally granular surface which was torn in some few places. In the cortex there were a few retention cysts. The stellate veins were not congested. The cortex was slightly thin, the line of demarcation between cortex and medulla was faint. The glomeruli and interlobular vessels were congested. The pelvis seemed to be healthy The right kidney resembled in all respects the left except that it was slightly larger, also there was more evident congestion in it.

The heart was quite large and the right side was moderately dilated, particularly the auricle. The epicardium was smooth. The subepicardial fat was somewhat increased in amount. On the anterior aspect of the left ventricle near the apex, was an area over which the epicardium was distinctly thickened and this area, to the fingers, felt as though the wall of the heart were thin, and almost as though the fingers could be forced through the wall. The pulmonary and tricuspid valves were healthy. There was perhaps a slight thickening of the edges of the tricuspid valve but it was not unusual. The foramen ovale was closed. The tip of the left ventricle was dilated and the area of dilatation was filled with old thrombi, some of which were softened. About this cardiac aneurism, the endocardium was exceedingly sclerotic. The columnæ carneæ which had evidently been hypertrophied, were evidently completely replaced by fibrous tissue and the dilatation had extended in such a way that some of these

fibrotic columns formed trabeculæ across the aneurism. The aortic orifice was not dilated and the valves were not very much changed, although they were somewhat fibrotic. There was no evidence, however, from the appearances of an insufficiency. The valves were competent to the water test. Beginning in the transverse arch of the aorta and extending down into the iliacs, the whole vessel was the seat of an exceedingly well marked diffuse luetic mesaortitis. In the ascending part of the arch there seemed to be nothing but some patches of fatty degeneration. The coronaries showed a very well-marked patchy arteriosclerosis. In some places the vessels were almost free from sclerotic changes; in others, the tip of a fine probe could barely be passed through.

The liver was of fair size and exceedingly flabby. The lower margin of the right lobe of the liver was deformed by scar tissue and the capsule was thickened. Scattered here and there upon the surface of both lobes were small nodules measuring not more than ½ cm. in diameter, two or three of them raised above the surface with an area of contraction about them. Other areas of the same general appearance did not seem to be raised above the surface and had no contraction about them. In several instances there were stellate scars which extended into the liver substance. On section, the organ showed evidence of a moderate degree of passive congestion. The surface was rather deeply congested and there was evidence of a considerable amount of fatty degeneration. The whole organ was exceedingly edematous. The gall bladder was small, the walls were thickened moderately, particularly the peritoneal surface which was definitely sclerotic and in the gall bladder was an ovoid cholesterin calculus.

The right lung was of fair size, the pleura for the most part was smooth. At one point on the posterolateral inferior edge of the upper lobe was an area of almost complete consolidation over which there was a fine fibrinous exudate upon the pleura. On cross section, this area had a congested granular surface. It had a somewhat wedge-shaped form and seemed to represent a focus of acute lobular consolidation. There were apparently no thrombi in the vessels leading to it. The rest of the lung tissue was only moderately congested and scarcely edematous. The apex was scarred. The left lung showed almost a completely atelectatic and scarred lower lobe, and an almost completely normal upper lobe. The apex was irregularly scarred, irregularly contracted. On section, it was distinctly meaty, very firm and within the substance there were small areas of purulent infiltration.

The stomach was generally congested, there was something of a morocco leather appearance throughout the mucous membrane and an increase in amount of mucus on the surface between the rugæ. On stretching the stomach, the rugæ could be almost completely flattened. There was nothing unusual in the duodenum which was also congested.

The pancreas was distinctly congested but showed nothing else abnormal. The intestinal tract showed an increase in mucus on the surface, was somewhat edematous and somewhat, particularly in patches, congested. The contents of the intestines were bile-stained. There was a moderate degree of hyperplasia of the solitary follicles. In the large intestines, particularly in the cecum, there was a definite diphtheroid exudate upon the surface.

This extended to a lesser degree throughout the rest of the large intestines. In the sigmoid there were numbers of diverticula.

ANATOMIC DIAGNOSIS.—Syphilitic mesaortitis; peripheral arteriosclerosis affecting particularly the coronaries, renals, and cerebral vessels; partial cardiac aneurism; hypertrophy and dilatation of the heart; myocardial fibrosis; edema of the brain; chronic diffuse nephritis; passive congestion of the liver, kidney, spleen and pancreas; acute lobular pneumonia; pulmonary atelactasis; chronic catarrhal gastritis; chronic follicular enteritis; acute diphtheroid colitis; pediculosis; scoliosis; cholelithiasis.

REMARKS.—In this case the basis of the myocardial changes seemed to rest upon a luetic process which had produced very definite coronary changes together with myocardial fibrosis. This latter may have been due either to the infection, or to the coronary condition, or, more probably, to both. There were

Fig. 2.—Case A-4464. (Case II.) In this case the heart is apparently elongated and immediately at the apex is the irregular slit indicating the point of rupture of the aneurismal sac which produced the appearance of increased length.

no pericardial adhesions, but the endocardium and epicardium were hyperplastic, conditions which prevented rupture of the aneurism. Evidently the thrombi within the sac were not essential in offering resistance to rupture, for they were softened. Death in this case was evidently directly associated with the lobular pneumonia, which, with the acute pseudomembranous colitis, may be looked upon as evidences of a terminal infection.

CASE II.

E. T., No. A-4464, was brought to the Receiving Ward of the Cincinnati General Hospital, as an emergency case, on June 30, 1916. He died within a few minutes after arriving at the hospital. No clinical history was obtained.

AUTOPSY PROTOCOL, (M., J. S.)—The body was that of a well developed, well preserved, white man about 50 years of age. Postmortem rigidity was exceed-

ingly well marked and lividity was present in the dependent portions. The pupils were equal and dilated. The teeth were discolored though in fair condition, and the gums were pyorrheic. The lips were cyanotic. The chest was barrel-shaped, the abdomen somewhat pendulous, and the superficial veins were slightly distended. Both ankles seemed enlarged, and the right seemed to have undergone some bony ankylosis, as it could not be moved.

The subcutaneous fat was abundant and the superficial muscles were well developed. Upon removing the sternum, the lungs partially collapsed. There were about 500 c.c. of a slightly blood-tinged fluid in each pleural cavity. There were no pleural adhesions in the left cavity. From the right anterior axillary line to the vertebral border and as far upward as the third rib, the right lung was adherent by fibrous adhesions. The mediastinal and pericardial fat was very abundant. When the pericardial sac was opened, a large quantity of blood-tinged fluid and clot flowed out. The amount of blood in the pericardial cavity was about 20 ounces. The omentum was filled with fat and the mesentery similary contained a great amount of fat. Around the cecum there were numerous old fibrous adhesions and the appendix was adherent behind the ileum and was represented by a short fibrous tag containing no lumen. There was no fluid in the abdominal cavity. There were no adhesions about the gall bladder.

The left lung was voluminous and crepitated throughout. There were a few small shotty areas beneath the pleura which no section represented obsolescent calcified tubercles. The cut surface of the lung showed no gross abnormality. The right lung contained the remains of numerous fibrous pleuritic tags. The lower lobe was soft, and friable, but crepitated throughout. This lobe was considerably congested and edematous and was the only portion of the lung that showed any pathologic change.

The heart was about twice its normal size. There were numerous old fibrinous adhesions between the epicardium and the pericardium. These adhesions were very short (⅛ inch) and drew the myocardium out into a small aneurism. The apex of the left ventricle had ruptured; the site of rupture occurring in a thin aneurismal sac measuring about 2 inches in diameter, the walls of the sac being represented evidently by fibrous tissue lined by endocardium throughout. Over the epicardium covering the sac, were numerous blood clots undergoing organization and the endothelial lining of these contained a number of small fibrinous vegetations. The heart and aorta were not opened but were sent to the museum intact.

The liver was about of normal size; it had an irregularly granular surface of a pinkish-blue color. It cut with increased resistance and the cut surface was purplish-red in color, and showed an increase in both fibrous and fatty tissue; the lobules stood out prominently, due to fibrous contraction. The gall bladder contained about twelve black, irregularly shaped concretions, all of about the same size. The concretions were rather soft. There was present in the gall bladder about 1 ounce of greenish-black fluid.

The kidneys were slightly enlarged. The capsules stripped with some difficulty leaving a mottled surface on which the stellate veins appeared moderately congested. The cortex was diminished in thickness and the line of demarcation between cortex and medulla was lost. The glomeruli were visible as red con-

gested points. The interlobular veins were congested. The renal pelvic fat was greatly increased.

The spleen was greatly enlarged. Upon the upper surface there was a large cyst containing about 500 c.c. of a clear straw-colored fluid. The inner lining of the cyst was thin, pale and glistening and was thrown into folds which readily disappeared on stretching. The cyst did not extend into the substance of the spleen, but lay within the capsule. The cut surface was soft and pulpy and very friable.

ANATOMIC DIAGNOSIS.—Ruptured cardiac aneurism; cyst of the spleen; chronic diffuse nephritis (interstitial type); acute splenic tumor; cirrhosis of the liver; absolescent pulmonary tuberculosis.

REMARKS.—This case illustrates again the abrupt termination in cases of cardiac aneurisms when the dilated portion of the myocardium is not protected by ventricular thrombi or pericardial adhesions. It also illustrates a condition of affairs which has given rise to much discussion, namely, one in which there are a few pericardial adhesions which it has been suggested have been an important factor in the production of dilatation by exerting traction on the cardiac wall. Diverticula of other organs,—esophagus and intestines,—are sometimes caused in this way, hence the term "traction diverticula." Whether or not traction was an important factor in this case cannot be stated, though the facts suggest it.

CASE III.

B. F., No. 3708, was admitted to the Cincinnati General Hospital on July 29, 1915. He died on November 4, 1915. The clinical history has been lost.

AUTOPSY PROTOCOL.—The body was that of an old gray-haired man, 5 feet tall. It was evidently, though not markedly, bowed forward. It was, as to the upper part, rather illy nourished; as to the lower, well supplied with fatty tissue. Rigor mortis was incomplete. Lividity was brilliant. To the left of the coccyx was a superficial bedsore 6x4 cm. in diameter. Five centimeters below the left great trochanter was a second bedsore, round, punched-out in appearance, its base on the muscle and its sides sharp and clean. It measured 4 cm. in diameter. The left leg, commencing 17 cm. below the great trochanter, was greenish, a hue that increased as the foot was approached, until in the foot itself, it was a blackish green and showed evidence of liquefaction necrosis. The terminal half of the foot had been amputated and at the site of the operation, the necrotic metatarsal bones protruded from the surrounding foul greenish dead tissues. The right leg had suffered not at all though the right foot in the region covering the os calcis laterally and on the plantar surface, was gangrenous. Just below the external malleolus was a deep penetrating ulcer 6x2 cm. Under the internal malleolus was a second, round one 2.5 cm. in diameter.

The interesting feature of this case was the cardiovascular system. The heart was enlarged and dilated especially on the right side, but also considerably on the left. The muscle was brown. Upon the anterior surface of the left ventricle near the base medially, was an area which to the touch suggested the presence of bone in the myocardium. Scattered about this, were numerous myocardial scars showing as pale striated areas beneath the epicardium. The

left coronary was exceedingly firm and very sclerotic. It was so thick and impregnated with lime salts that it was opened with difficulty. The left branch of the descending branch of the left coronary was also exceedingly sclerotic and almost obliterated. It was this branch which led directly to the firm area mentioned above. When the ventricle was opened, it appeared at once that the area of hardening, which measured some 3½ cm. in diameter, was actually a very thin lamella of fibrotic myocardium not more than 1 mm. in thickness and densely filled with lime salts. The endocardium of both ventricles was fibrotic and the columnæ carneæ and papillary tendons were also sclerotic. The valves were not especially damaged though they were slightly fibrotic. The aorta also was not remarkably affected. At but one point in the arch was there a well marked area of atheroma, though there were a number of fatty areas of degeneration in the intima. The main branches of the aorta were, however, more affected by the sclerotic process, and this was especially true of the main branches of the subclavians, and of the iliacs. The spermatics, internal epigastrics, obturators, profundas and the femorals, popliteals, and their terminal branches all simulated calcified tracheas, and this was especially noticeable in the left leg. Here, the popliteal was almost completely obliterated just above the origin of the anterior tibia.

The lungs were very healthy in general appearance, although the left was almost completely adherent to the mediastinal tissues and to the parietes. Nevertheless on section they were pale and dry and had no areas of consolidation.

The liver weighed 1175 grams, and was pale brownish yellow, nodulated and sclerotic. The bile ducts were patent.

The spleen (120 grams) was flabby, the edges rounded, the capsule thickened at scattered points, and the pulp slightly fibrous, showing enlarged Malpighian corpuscles.

The pancreas, aside from a very definite fatty infiltration, showed no microscopic changes.

The kidneys (left 120, right 90 grams) were small, granular and pale. Each showed the remains of fetal lobulation. To each the capsule was moderately adherent. The cortices were thin and gray, the medullæ fibrous.

The adrenals showed increase of medullary tissue with focal accumulations of cortical tissue simulating adenomas. The pelves of the kidneys and the ureters were healthy. The bladder was contracted and held an ounce or so of a cloudy urinous fluid. The mucous membrane was intensely reddened, and thickened. Upon a number of the folds were patches of fibrin forming white points. The urethra was not inflamed. The prostate was small and fibrotic. Both testicles were very small, scarcely larger than ordinary ripe olives.

The brain was exceedingly edematous. There were patches of arteriosclerosis in the arteries of the base, but no evidence of blocking of the lumens.

Anatomic Diagnosis.—Diffuse peripheral arteriosclerosis; coronary arteriosclerosis; gangrene of right leg, and left foot (partial); partial cardiac aneurism; atrophic cirrhosis of the liver; myocardial fibrosis; cardiac hypertrophy and dilatation; fatty infiltration of the pancreas; edema of the brain; arteriosclerotic kidneys; acute catarrhal cystitis; atrophy of the testicles.

Remarks.—This case illustrates a relatively rare location of a cardiac

aneurism, and it also illustrates typically what may happen to a section of myocardium whose blood supply is so gradually decreased that the functional tissue is completely replaced by fibrous tissue, and in which the fibrous tissue later becomes infiltrated with lime salts.

In this case the changes in all the organs are predominantly sclerotic which indicate the presence of very general vascular changes. The slow progress of this condition is indicated in the age of the patient.

CASE IV.

C. G., No. 6136, was admitted to the Cincinnati General Hospital on November 24, 1915. He died on December 22, 1915.

CLINICAL NOTES.—The patient came to the hospital complaining of short-

Fig. 3.—Case 6136. (Case IV.) Note the lamellated clot more than half filling the left ventricle, and also note the extreme fibrosis of the ventricular myocardium. At the tip of the ventricle the clots fill the meshes of the fibrotic myocardial wall.

ness of breath. He had previously been in the hospital from October 15, 1915, to October 27, 1915.

For a year he had felt under the weather. He had been a heavy drinker of spirits, but denied venereal infection. The difficulty of which he complained troubled him for at least a year, during which time he was especially uncomfortable at night. For three months he reacted badly to the slightest exertion. With this he had a dry cough. Two weeks before his first admission he spat up a little frothy, pale red, bloody fluid. For six monnths he had some edema of the feet and legs, and for some months had urinated frequently. For two weeks he had an edema of the external genitalia. His bowels were regular.

On October 17, the following note was made: Pupils equal; right radial pulse stronger than the left which is almost imperceptible. Apex beat visible and palpable to the left of the nipple in the fifth interspace; impulse strong and heaving. The first sound at the apex is reduplicated; the second pulmonic

slightly accentuated. There are no audible murmurs. There was visible pulsation in the first interspace and well marked retrosternal dullness. There was no tracheal tug. The legs below the knees were moderately edematous.

Relative cardiac dullness:

First interspace	2.3	cm.	to right.
	2.5	"	" left.
Second interspace	2.8	cm.	to right.
	3.3	"	" left.

Blood pressure: Right arm—systolic 156, diastolic 125.
Left " — " 144, " 120.

The radiographic report on October 20th was as follows: "The heart is lying in a transverse position. Its long diameter has apparently increased. Upper mediastinal shadow is broader than usual and from the relation of its curves suggests an enlargement of the aortic arch." A fluoroscopic examination of the chest revealed no circumscribed enlargement of the aortic arch, but instead, a diffuse enlargement suggesting a dilatation of the aorta.

The Wassermann reaction was negative.

During his stay in the hospital his temperature remained normal except for an occasional rise to 99.5° (maximum). Pulses remained between 60 and 100; respiration, 20 — 30.

He was discharged, unimproved, at his own request on October 27, 1915.

At the time of his second admission on November 24, 1915, the patient was generally edematous, and exhibited Cheyne-Stokes breathing. His urine contained albumin and casts. Over the base of each lung there were signs of edema. The heart was enlarged; 15 cm. to the left; 3 cm. to the right. The cardiac rhythm was irregular. A faint systolic bruit was heard just below the left nipple.

As time went on there was no improvement. The patient was drowsy most of the time; Cheyne-Stokes breathing persisted; the pulse became gradually weaker, and death occurred on December 22.

CLINICAL DIAGNOSIS.—Dilatation of the aorta; arteriosclerosis; chronic diffuse nephritis; myocardial insufficiency; mitral insufficiency.

AUTOPSY PROTOCOL (G.)—The body was that of a well developed, poorly nourished negro, apparently about 50 years old, and six feet tall. The extremities were edematous. The teeth were in exceedingly poor condition, those that were present,—two above and seven below. The right pupil was twice the size of the left.

When the chest was opened the lungs did not collapse; each pleura contained about 500 c.c. of clear fluid, and no adhesions. Both lungs were congested and edematous. The left showed an apical scar. In the right lung, in the lower lobe was an area of consolidation about the size of a hen's egg.

The pericardial fluid was not increased. The heart was markedly enlarged and also dilated, the latter condition being especially prominent in the right ventricle. The tricuspid valves were thickened and fibrotic. The left ventricle was exceedingly hypertrophied, and near the apex was a mass of thrombus attached to the myocardium which was extremely thin and fibroid. The myocardium was, generally, the seat of a well marked fibrosis. The aortic valves were

slightly thickened, and the aorta showed, especially about the mouths of the coronaries, thickening and many scattered patches of atheroma. Subintimal fatty changes were especially prominent. The whole aorta, but particularly the arch, was somewhat, though not strikingly dilated. The mitral valve was sclerotic, and the leaflets much thickened.

The peritoneal cavity contained a small amount of free fluid. The mesenteric glands were enlarged and firm, but showed no visible evidences of disease. The stomach, liver and spleen were congested. The liver was of normal size but unusually firm. The pancreas, intestines and adrenals were not unusual. The ureters, bladder and prostate showed nothing of note.

The kidneys were small and scarred as if by healed infarcts. The capsules stripped readily leaving somewhat granular surfaces. The cortices were narrowed, and there was some evidence of sclerosis.

Permission to remove the brain was not given.

ANATOMIC DIAGNOSIS.—Chronic diffuse nephritis; myocardial fibrosis; cardiac thrombosis; cardiac hypertrophy and dilatation; aortic dilatation; aortic atherosclerosis; terminal lobular pneumonia; congestion of lungs, liver, spleen and stomach; anasarca.

REMARKS.—This case offers an exceedingly good illustration of what happens in preparation for, and prevention of, cardiac aneurisms. The whole myocardium was the seat of an extensive very diffuse fibrosis, which had been accentuated near the apex of the left ventricle. At that place the wall of the cavity was composed almost entirely of fibrous tissue, and was, compared with the rest of the myocardium, very thin. Evidently there had been the tendency for the heart to bulge out at this point. But during the period of incipient bulging, thrombosis had occurred, and over the whole area of thinning, clots had been laid down forming lamellæ which had been sufficiently firm to protect the ventricular wall. It seems reasonable to expect that, had the myocardium as a whole been more vigorous; had there been a higher blood pressure, and, therefore, a more rapid stream of blood, a more distinct bulging would have been produced.

CASE V.

CLINICAL NOTES.—M. G., hospital No. A-6479, a colored female, aged 35, married, a washwoman, was admitted to the Cincinnati General Hospital, September 30th, 1916, complaining of "shortness of breath, and swelling of the legs and stomach."

Family History.—The patient's mother died of dropsy at the age of 55 years.

Past History.—The patient had "measles," "mumps" and "whooping cough" in childhood. She had arthritis of both ankles, with swelling and pain, after she was grown. She denied having had venereal infections. The patient said she used to drink about three glasses of beer daily but no whiskey until six months ago. She did not use tobacco, or drugs. She had two children, aged 18 and 5 years, both living and well. The patient was in the hospital last Spring and at that time she was emaciated. She complained of pain in the epigastrium. There was a tumor just to the left of the median line and above the navel. This was

about the size of a pigeon's egg, or larger. It had a pulsation which at times seemed to be expansile although the tumor and pain disappeared on the administration of iodide potassium in large doses and the patient was discharged after a few weeks, feeling well.

Present Illness.—The patient has been feeling badly ever since the first of September. She had had shortness of breath on the least exertion. She frequently has had to sit up at night because of dyspnea. About a week after the onset her feet began to swell. The swelling has gradually increased and the abdomen began to swell before she came to the hospital.

Physical Examination.—The patient's general condition was fair. The pupils were moderately dilated. They reacted to light and accommodation. There was no nystagmus. The conjunctivæ were slightly injected. The ears and nose were negative. The tongue was moist. Many teeth were missing. Those which remained were in poor condition. There was pyorrhea alveolaris. There was a general glandular enlargement, including the epitrochlears. The glands were only slightly enlarged and discrete. The thorax was symmetrical and expansion was equal. The lungs were negative on percussion and auscultation, except for slight dullness at the bases, without alteration in the signs on auscultation. The heart apex was one inch outside the mid-clavicular line. The cardiac dullness was not given. The rhythm was irregular. There was a systolic murmur

Fig. 4.—Case A-6479. (Case V.) In this case the heart was elongated and the tip bulbous. The aneurismal sac was well developed and filled with a recent red clot in which organization was commencing about the periphery.

at the apex which was also heard along the sternum with a diastolic murmur at the aortic area. The abdomen was distended. There was a movable dullness in the flanks. There was moderate edema in the lower extremities. The reflexes were normal.

A Wassermann reaction was positive. The sputum was examined for tubercle bacilli, and none were found. The urine was yellow. Specific gravity 1.010, slightly acid, albumin present. There was no sugar. Microscopically granular and hyaline casts and leucocytes were found.

On October 10th, the patient had improved very much. The edema of the lower extremities had practically disappeared and the dyspnea was less marked. On the 19th, she had continued to improve. The edema had disappeared and she was allowed to be up for an hour. On October 25th, the patient wakened suddenly about 5 o'clock in the morning complaining of a very severe, sharp, continuous pain in her abdomen. She was found in a sitting posture and had both hands on the abdomen. She was also vomiting at times. On examination there was some distension of the abdomen but no apparent localized tenderness although she complained of pain in the right upper quadrant. There was no rigidity and no masses palpable in the abdomen. The following day she still complained of pain in the abdomen. There was rigidity in the upper right quadrant. The liver was enlarged a finger breadth below the costal margin. On November 9th, the apex impulse was diffuse, most marked in the sixth interspace, 7 inches from the mid line. Relative cardiac dullness extended 8 inches to the left in the seventh, 7 inches in the sixth, and 6½ inches in the fifth. The dullness to the right was not given. In the seventh interspace retraction was noticed during each systole. No murmurs were heard at the apex. There was a faint diastolic and a blowing systolic murmur at the base. Traubes' space was dull. The liver was 11 cm. below the xiphoid cartilage and 5 cm. below the costal margin in the nipple line. On November 12th, a catheterized specimen of urine showed 2 grams of albumin per liter with numerous hyaline and some cellular casts, also granular casts and pus cells. Moist rales were heard at the base of each lung. November 13th—aspiration of the pericardium yielded 6 ounces of bloody viscid fluid.

X-ray examination of the gastrointestinal tract on October 10th, was entirely negative.

On November 8th, there was marked increase in the transverse diameter of the heart, especially involving the left ventricle. Fluoroscopic examination of the chest showed the transverse diameter of the heart markedly increased in width, the right side of which does not pulsate.

The patient's temperature was for the most part normal or subnormal with occasional rises to 99° or 99.6.° The pulse was between 80 and 100, respiration 120 two days before death. Respirations were between 20 and 30.

Clinical Diagnosis.—Nephritis; cardiac hypertrophy and dilatation; aortic insufficiency; pericardial effusion; passive congestion of the liver; ascites, general anasarca; passive congestion of posterior lower lobes of the lung; uremia; syphilis; hemopericardium.

Autopsy Protocol (G. G.)—*Necropsy.*—The body was that of a well

nourished negress about the age of 35. Postmortem rigidity was very slight and there was slight lividity in the dependent portions. Over the left hip was a linear scar which ran horizontally and was about 3 inches long. There was a small trochar wound about 1 inch to the left of the midsternal line and in the fourth interspace. The teeth were in poor condition, the majority were present but many were in a carious condition. The eyes were equal; the pupils were not dilated but there was present an internal squint of the right eye. The lower extremities on both sides showed some edema. The subcutaneous tissues were very moist and edematous over the whole abdomen and chest. The musculature of the abdomen was very poorly developed. There was an area of interstitial hemorrhage just beneath the trochar wound about 3 inches long and 2½ inches wide. When the abdominal cavity was opened it was found to be filled with a straw-colored fluid. The stomach was distended but the small intestines were contracted and the bladder was about empty. The peritoneum was very much injected and both the lesser and greater omentum were deeply injected. The appendix was *in situ* and apparently healthy. There were many adhesions between the anterior surface of the right and left lobes of the liver and the abdominal wall. The left pleural cavity was fairly free from adhesions but there was present about 4 ounces of a bloody fluid. When the chest was opened, the left lung did not collapse but the right did. On the surface of the pericardium beneath the point of the trochar wound was another interstitial hemorrhage of about 3 inches in diameter. The pericardium was filled with about 8 ounces of a bloody fluid. The pericardial cavity contained numerous adhesions mostly about the apex.

The ascending colon was firmly fixed to the right kidney. Both kidneys were strongly adherent to the posterior abdominal wall and were with difficulty removed. The right was found adherent to the ascending colon and also to the posterior wall. Extending down into the iliac fossa there was found a tissue that resembled to some extent adrenal tissue and which infiltrated all the interstitial tissues of the groin and to some extent was found within the anterior abdominal wall. This was true of both sides but was more extensive on the right than on the left. The stomach was injected and there was a slight excess of mucous material on the surface. The rugæ were not very apparent and the mucosa of the stomach presented the appearance of morocco leather. Otherwise the organ was normal. The duodenum was quite intensely injected and there were several small hemorrhages in the lower part of the duodenum. There was nothing more than edema and congestion of the gastrointestinal tract. The heart measured 18 cm. from the root of the aorta to the apex, and had a generally blunt cylindrical form. The whole apical region was somewhat bulbous and was separated to a certain extent from the rest of the heart by a slight groove about 6 cm. above the apex. This bulbous apical region had a semifluctuating feel which suggested the presence of an aneurism at the apex. The whole pericardium was roughened and covered with the tags of old adhesions in which there were occasional small areas of hemorrhage. At one point just about the middle of the surface of the right auricle was a fine puncture wound surrounded by an areola of extrava-

sated blood which measured about 3 cm. in diameter. This puncture wound apparently extended completely through the myocardium into the cavity of the right ventricle where it impinged upon a small mass of mural thrombi. The right auricle was very considerably dilated and in the auricular appendage there were a few old mural thrombi. There was a certain amount of jaundiced appearance in the mural endocardium, an appearance which was also seen to a somewhat less extent in the vessels. The right ventricle was relatively contracted. The endocardium along its left posterior side was fibrotic and milky and the papillary muscle of the left tricuspid leaflet were fibrotic. In the tip of the right ventricle there were masses of old mural thrombi. The left auricle was somewhat dilated but aside from hemolytic pigmentation or staining showed no unusual appearances. The mitral valve was evidently not dilated. The left ventricle was tremendously dilated but was filled almost completely with a laminated clot which was rather firm peripherally but quite soft centrally. This clot reached almost to the aortic valves. Apically the myocardium was replaced by a thin zone of connective tissue from two to three mm. thick. Nearer the base of the heart the myocardium became about 15 mm. thick and showed some evidence of hypertrophy. The mitral papillary muscles and the ventricular myocardium were distinctly fibrotic. The mitral valve leaflets showed no changes on the margins and the chordæ tendineal were not contracted. The aortic leaflets were apparently healthy and the orifice was sufficient by the water test. The aorta itself showed some slight patches of subintimal hyperplasia and some slight puckering of the intima. These changes were shown particularly in the transverse arch just in the neighborhood of the great vessels. Were it not for the hemolytic staining, these patches would be typical luetic ones. Aside from that, the aorta showed no changes. There were no dilatations and no sclerosis. The peribronchial glands showed some calcification. The coronaries were, in their basillar segments at least, thin and normal in appearance. A fine probe could be passed however but 5 cm. down the descending branch of the left coronary at which point this vessel seemed to be sclerotic. Sections from this part of the coronary were saved for examination. Below this point the pericardium seemed to be far more thickened than about the base and the path of the vessel could not be distinguished in the hyaline connective tissue.

The left lung had a rather firm feel and its outer surface was dark gray in color. The cut surface of the lung showed an intense congestion and edema, more intense to the center and decreasing towards the periphery. The right lung was more contracted than the left, had a distinct meaty feel and did not crepitate in any portion. On the inner border of the middle lobe was found a dark consolidated area which on section proved to be an infarct. This infarct measured about 2½ inches from the border to the apex of the triangle and about 2 inches high along the border of the lung. The cut portions of the lung showed only edema and congestion. The upper lobe of the right lung was fairly healthy and showed very slight if any congestion.

The liver showed a dirty brown grayish appearance, its edges were sharp and irregular and the whole organ was decreased in size and very flabby. Over

the surface were found many areas of a yellowish color and many fibrous tags. The organ cut rather firm and on section there were found the typical patches of passive congestion with areas of fatty degeneration. The cut surface of the organ was of a yellowish-reddish brown color. The gall bladder was filled with a brownish, almost clear mucous fluid in which there were found no stones nor any gravel.

The spleen was hard, contracted and had a very fibrous feel. The pulp was of a deep red and there was an evident increase in fibrous tissue.

The right kidney was firm and generally pale. The capsule was quite firmly adherent by evidently recent fibrous and some fibrinous adhesions. When the capsule was removed, it was seen that the capsule was massively filled with hemorrhagic patches some of them petechial, most of them larger and confluent. Not only was the capsule involved in this process but also the perirenal tissues which had a distinctly indurated feel and in which the fat at certain points had a peculiar orange appearance which suggested congested thymus tissue. The surface of the kidney was generally yellow with massive and small petechial hemorrhages scattered generally over the surface. On section, the kidney appeared to be completely infarcted, and section of the renal artery showed a mass of thrombotic material almost completely blocking the vessel. The whole cut surface of the kidney was jaundiced and in the regions where the infarction had not been complete the substance was distinctly pinkish-gray. The left kidney was about the same size as the right. The capsule removed with fair ease leaving a very finely, indistinctly granular surface upon which the fetal lobulations were very distinct. The whole organ was rather firm, decidedly edematous, the stellate veins were not congested. On section, it appeared that the cortex was increased in thickness, there was some evidence of a moderate sclerosis in the pyramids, the line of demarkation between cortex and medulla was fairly distinct and showed some evidence of fibrosis and was distinctly jaundiced; the glomeruli could be seen fairly well as congested points and the interlobular vessels were injected. There was no evidence of thrombosis or infarction in this organ. The blood vessels, especially the arteries, were deeply jaundiced.

Anatomic Diagnosis.—Aneurism and thrombi of the left ventricle; fibrosis of the left auricular walls, mitral valve and papillary muscles of the left ventricle; trochar puncture wound of the heart; congestion and edema of all the viscera; pulmonary infarct; complete infarction of the right kidney; acute diffuse nephritis of the left; chronic passive congestion of the liver.

Remarks.—This case represents the type in which a moderately large area of the ventricular muscle was damaged, and in which the intracardiac pressure was not excessive. The result was, therefore, that a very considerable gradual dilatation occurred. No thrombi were formed in this aneurism until a short time before death and then the sac was rapidly filled with clot which reached almost to the valves. From this thrombotic mass, a large bit was carried to the kidney where it completely blocked the renal artery.

SUMMARY.

The series of cases reported in this paper has to do with the formation of cardiac aneurisms. Cardiac aneurisms and aortic aneurisms resemble one another in every aspect so far as pathogenesis is concerned and differ only in the fact that they appear in different organs.

One of the cases reported showed the beneficial result of thrombosis in a heart which otherwise might have developed an aneurism (6136); one showed an early stage of aneurism formation near the apex (A-2775); one showed an early stage of aneurism formation in an unusual situation, and also illustrated calcification of the fibrous tissue forming the wall of the sac (3708); one showed a rupture of a chronic aneurism in spite of a few pericardial adhesions; and one showed a fully developed large chronic aneurism (A-6479).

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A STUDY OF THE OCCURRENCE OF IMMATURE POLYNUCLEAR LEUCOCYTES IN THE CIRCULATING BLOOD IN PULMONARY TUBERCULOSIS AND OTHER INFECTIOUS DISEASES*

By Alex. M. Burgess, M.D., Providence, R. I.

AMONG the many investigations of the activities of the polymorphonuclear leucocyte, those of greatest interest to the clinician have dealt with the relation of the leucocyte to the common infections. In the study of clinical cases, the estimation of the leucocyte count and the examination of the stained blood film have long been routine procedures. More recently variations in the morphology of the polynuclear leucocytes in the blood stream have been recognized as occurring in certain diseases, and attempts have been made to determine the relation of these changes to the clinical condition.

Arneth, in 1905, classified the polynuclear leucocytes of the circulating blood according to the number of lobulations of their nuclei, and noted that in infectious diseases, especially tuberculosis, the proportion of the cells of Classes I and II, those with single or two lobed nuclei, was increased. This he interpreted to mean that the younger, immature leucocytes were relatively more numerous than in the normal blood. For example, the following represent respectively a normal count, and one which might occur in such an infectious disease as tuberculosis:

	CLASS I.	CLASS II.	CLASS III.	CLASS IV.	CLASS V.
Normal:	12	35	30	18	5
Abnormal:	52	37	10	1	0

*I am indebted to Dr. W. P. Buffum, Jr., and Mr. John von der Leith for aid in making some of the blood examinations.

A count like the second of these, Arneth calls "a shift to the left," a shift of the majority to Classes I and II.

It was noted by Arneth that in active pulmonary tuberculosis, although leucocytosis was absent, a well marked "shift to the left" usually occurred. He supposed that the relatively immature cells of Classes I and II were less able to cope with an infection, and that therefore the resistance of a patient who showed such a "shift" must be lowered and the prognosis must be poor.

Arneth's classification has been widely used by many investigators, especially in the study of pulmonary tuberculosis. Opinions of its value vary greatly, and on reading the literature one is led to suspect that its true significance is not appreciated. P. H. Ringer, for example, says "It must be distinctly understood that the Arneth blood picture can in no way be taken to indicate the amount of lung involvement or the stage of the disease. It is simply and solely an index of the resisting power of the patient." R. S. Cummings regards it of no diagnostic worth, and of value in prognosis in doubtful cases only. The opinion of Solis-Cohen and Strickler is that "Few that take up the study of the picture carefully ever abandon it entirely, but he who places implicit confidence in its readings and bases his prognostic opinion chiefly thereon will not infrequently be led into error." More unfavorable is the statement of Bushnell and Treuholtz that "In advanced and active tuberculosis the method of Arneth gives us as a rule no information which we do not already possess."

In view of the essentially vague opinions as to the significance and value of the Arneth method, it seemed possible to the writer that a study of the leucocyte picture in pulmonary tuberculosis and other infections, and a careful correlation of this picture in the cases studied to other clinical and pathological facts, might yield information of interest. Therefore, counts were made on a number of patients with pulmonary tuberculosis and on cases of other infectious diseases as they were encountered in the routine of clinical work, and so far as possible the nature and degree of activity of the lesion was determined. In a few cases of fatal pulmonary tuberculosis a postmortem study of the bone marrow was carried out.

It became apparent at once in making leucocyte classification that the personal element must be a factor which causes great variation in results. Ringer states that he counts as one, two nuclear lobes connected by an isthmus of nuclear material "a third or more the thickness of the nucleus," and as two, lobes connected by a narrower strand. He also counts superimposed nuclei as separate units. Certain other observers insist that to be counted as separate, lobes must have only a minute thread-like strand connecting them, and that when nuclei are superimposed they must be counted as one, or else the cell must be left unclassified. It has seemed to the writer that the latter method allowed of far less personal variation in making the estimations, and it has therefore been followed. All doubtful cells have been disregarded. In the results herewith presented it will be noted that the normal cases show a larger proportion of cells in Classes I and II than do the normal counts published by many other observers; but it is probable that this can be explained as due entirely to the personal interpretation of the rules used in classifying the cells. Ordinary

Case No.	Disease	White Count	Arneth Count					Ratio	Remarks as to Clinical Condition, Temperature, etc.
			I	II	III	IV	V		
1	Normal		29	40	29	2	0	0.4	Normal.
2	"		35	40	10	4	0	0.65	"
3	"		28	45	15	1	0	0.46	"
4	"		17	31	32	10	0	0.23	"
5	"	8,200	28	42	25	5	1	0.38	"
6	"	6,000	30	32	22	2	0	0.54	"
7	"		4	27	5	1	0	0.12	"
8	"	9,000	38	43	15	4	0	0.61	"
9	"	9,500	59	72	14	0	0	0.68	"
	Av'ge of normal cases		30	41	19	2	0.1	0.48	
10	Pericarditis and nephritis	17,900	29	27	29	4	1	0.4	Temperature 100 to 101. Recovery in a few weeks.
11	Endocarditis (postrheumatic)	11,000	45	36	12	5	1	0.83	T. 99.5 to 100 for several weeks.
12	Alveolar abscess (small)	14,600	24	52	18	6	0	0.31	T. 99. General malaise and aches.
13	Acute appendicitis	20,000	66	91	37	5	1	0.49	T. 100. Operation. Inflamed appendix. No pus.
14	General myositis (Chronic).		45	35	14	5	1	0.81	T. 100. Gradual recovery.
15	Bronchiectasis (Improving).		50	54	19	4	0	0.65	T. normal. Feels well. Sputum slight.
16	Lobar pneumonia	28,000	124	26	3	0	0	4.2	Acute lobar pneumonia with recovery.
17	Mar. 3, pulmonary embolus c. sept. pneu.	31,000	73	19	7	1	0	2.7	Embolism following appendectomy. Markedly toxic.
	Mar. 8, pulmon'y abscess	16,000	84	12	4	0	0	5.2	Coughed up large quantities of foul pus.
	Mar. 12, pulmonary abscess with gangrene	12,000	93	8	0	0	0	12.3	T. septic in type 100-103. Large quantities of sputum. Oper'n 2 days later.
	Mar. 26	14,500	88	10	2	0	0	7.2	T. 98.6-100. Draining fair amount pus.
	April 22	14,000	45	35	17	4	0	0.8	T. normal. Wound not draining.
18	Bronchiectasis		108	16	5	0	0	5.1	Large quantities of purulent sputum.
19	Bronchiectasis (Question of T. B.)		83	66	7	2	0	1.1	Considerable purulent sputum.
20	Empyema	25,000	88	39	8	0	0	1.9	T. 100. Draining some pus from operation wound. Looks sick.
21	Empyema	19,000	68	31	1	0	0	2.1	T. 100 for 10 days.
22	Appendicitis	12,900	63	28	7	2	0	1.7	Operation 2 days later. Appendix apparently continuously discharging pus into cecum.
23	Carcinoma (abdominal)	25,000	104	47	14	2	0	1.6	Operation. Death. Specimen shows no necrosis. T. 100.5. Pulse 120, weak.
24	Mar. 16. Appendicitis. 9 days post operative	29,400	54	32	11	3	0	1.2	Wound draining. Temperature 100.4.
	Mar. 25. Improvement	14,600	48	38	9	5	0	0.9	Wound no longer draining.
	Mar. 31. Improvement	14,000	22	23	5	0	0	0.8	Wound no longer draining.
25	Malaria		63	36	1	0	0	1.2	
26	"		73	24	3	0	0	2.7	
	"	9,600	67	31	2	0	0	2.0	

Case No.	Disease	White Count	Arneth Count					Ratio	Remarks as to Clinical Condition, Temperature, etc.
			I	II	III	IV	V		
27	Pulmonary tuberculosis	.....	33	33	23	6	0	0.5	Arrested. T. normal. No sputum.
28	" "	.....	35	40	27	13	1	0.4	Chronic, very slowly progressive type. T. 97-99.
	" "	.....	85	57	16	2	0	1.1	Considerable sputum.
29	Dec. 16, '14, " "	.....	61	29	9	1	0	1.6	Chronic, very slowly progressive.
	Mar. 16, '15 " "	.....	82	33	5	1	0	2.1	Considerable sputum.
30	Nov. 14, '14 " "	.....	88	29	12	1	0	2.1	Chronic, very slowly progressive.
	Mar. 16, '15 " "	.....	77	36	6	0	0	1.8	Considerable sputum.
31	Jan. 12, '15 " "	7,000	102	30	9	1	0	2.5	Chronic, very slowly progressive.
	Mar. 16, '15 " "	.....	58	55	20	2	0	0.7	Sputum slight.
32	Dec. 14, '14 " "	.....	44	42	17	1	0	0.7	T. normal. No sputum.
	Mar. 15, '15 " "	.....	84	30	15	0	0	1.9	Slight activity.
33	Dec., '14 " "	.....	26	33	10	3	0	0.5	Chronic, slowly progressive. T. usually normal.
	Jan., '15 " "	.....	70	50	26	4	0	0.9	Sputum thick; 50 to 80 c.c. daily.
	Mar., '15 " "	.....	115	32	4	0	0	3.2	Sputum thick.
34	Jan., '15 " "	.....	83	47	14	1	0	1.3	Chronic, very slowly progressive.
	Mar., '15 " "	.....	94	44	4	0	0	1.9	
35	Nov., '14 " "	.....	49	34	21	0	0	0.9	Slowly progressive fibroid phthisis. Sputum abundant and increasing in amount.
	Dec., '14 " "	.....	94	33	8	0	0	2.3	
	Jan., '15 " "	9,000	110	22	3	0	0	4.4	
	Mar., '15 " "	.....	90	55	7	0	0	1.4	
36	Nov., '14 " "	.....	90	20	0	0	0	4.5	Chronic, progressive. High temperature. About 150 c. c. sputum. Chills.
	Dec., '14 " "	9,100	125	22	2	0	0	5.6	
	Jan., '15 " "	.....	115	26	0	0	0	4.4	
	Mar., '15 " "	.....	90	27	3	0	0	3.0	
37	Pulmonary tuberculosis c carcinoma of rectum..	.....	130	30	3	0	0	3.9	
38	Pulmonary tuberculosis	9,400	127	16	1	0	0	7.4	Rapidly progressive. Much sputum. Cavitation.
39	Jan. 5, '15 " "	16,400	92	63	6	1	0	1.3	Active and progressive.
	Jan. 8, '15 " "	8,400	103	44	16	1	0	1.7	High temperature.
40	Pulmonary tuberculosis	9,800	86	36	3	0	0	2.2	Acute exacerbation of chronic process. T. 98-101. Sputum.
41	Dec., '14 " "	.....	120	40	5	0	0	2.6	Temperature 102 irregular.
	Jan., '15 " "	8,100	103	31	3	0	0	3.0	Sputum scant and puriform. Temperature 102 sustained.
42	" "	8,200	112	28	10	1	0	2.9	In extremis. Sputum practically pure pus. Died 4 days later.
43	" "	.....	90	27	10	0	0	2.4	Septic type of temperature. Death in a few days.
44	" "	.....	70	11	1	0	0	5.8	In extremis. Sputum puriform and scant.
45	" "	.....	103	55	7	0	0	1.6	Incipient. Doing well until 2 days after this examination, when relapse occurred.
46	" "	16,000	95	21	9	0	0	3.1	Suspicious case which later turned out to be rapidly progressive and fatal.
47	" "	6,300	70	31	8	0	0	1.8	Question of incipient T. B. Rales at one apex. T. 99.

smear preparations stained with Wright's or Hasting's modification of the Romanowsky stain were used in every case.

In making the examinations of the stained specimens the writer became impressed with the difficulty which often arose in determining whether a given cell rightly belonged in Class II, III, IV, or V. It was, on the other hand, usually an easy matter to differentiate between cells of Class I (immature cells whose nuclei had not yet divided), and the more mature cells of the other classes which showed at least one true interlobular division. The study of the cases has, in the opinion of the writer, fully justified the plan of considering all undivided nuclei (Class I), as immature cells, and all divided nuclei, (Classes II, III, IV, and V), as mature cells, and of judging the degree of the "shift to the left" accordingly. The "Arneth index" as ordinarily used, has referred to the ratio between the number of cells which fall under Classes I and II, and those in Classes III, IV, and V. In the writer's opinion, however, a preponderance of the really immature leucocytes of Class I as opposed to all the other classes, is of more significance than is any variation between the proportion of the cells of the remaining classes, and it is believed that evidence in support of this opinion will be found in the data herewith presented.

The blood of forty-seven people was studied. Of these, nine were normal so far as infectious disease was concerned, seventeen were suffering from nontuberculous infections, and the remaining twenty-one, from pulmonary tuberculosis. The detailed results are given in the accompanying table.

In attempting to draw conclusions from the data presented, it may be well to review briefly some of the known facts regarding the activities of the polynuclear leucocytes. In health, the number of leucocytes in the circulating blood is maintained at a figure which varies between 5,000 and 10,000 per cubic millimeter. Of these, 60 to 70 per cent are polynuclears. Like most other cells, these leucocytes must be constantly dying or being destroyed, and as constantly replaced by new ones arising by cell division of their progenitors, the myelocytes of the bone marrow. In disease, the output of the bone marrow may be increased in two ways. First, it may be increased as the result of direct stimulation of the marrow by a toxic substance circulating in the blood, as in an acute streptococcus infection. In such a case the number of leucocytes in the circulating blood is markedly increased, and as the increase must be due to newly formed cells, a *slight* "shift to the left" of the Arneth formula occurs. Second, the output of the bone marrow may be augmented as a result of increased destruction of leucocytes. In such a condition as a tuberculous cavity in the lung the bone marrow is not specifically stimulated, but is merely attempting to replace the leucocytes which are constantly being destroyed or cast off. In this way the proportion of immature forms in the blood may be greatly increased, a *marked* "shift to the left," though no leucocytosis or even, indeed, a leucopenia results.

The toxin of the tubercle bacillus does not typically attract the polynuclear leucocyte. The histological work of Mallory clearly demonstrates that it is the endotheliocyte that is specifically attracted into the lesions of this disease. Furthermore, in tuberculosis a leucocytosis does not occur. When, however, the

tubercles become extensive, and necrosis and softening of the lesions occur, polynuclears invade the necrotic areas in very large numbers, apparently specifically attracted by the products of necrosis. When cavities are formed, and a large amount of sputum is discharged, enormous quantities of leucocytes are used up by actually being cast off from the body. The extreme "shift to the left" seen in such instances is illustrated by Cases 36 and 38 in the preceding tabulation. The bone marrow, stimulated by the abnormal withdrawal of leucocytes from the circulation, is forced to put out a large number of young cells into the blood stream.

When the increased demand on the bone marrow for polynuclear leucocytes has remained at the same point for a long time, hyperplasia occurs, as it does in the case of other overworked tissues. This is shown by an extension of the red bone marrow into the shafts of the long bones. As a result of this formation of new bone marrow the supply of leucocytes is increased to meet the demand, and it is no longer necessary for the marrow to put out immature cells. Under such conditions, with the extension of the bone marrow, the Arneth picture may return to normal, as is illustrated by Cases 28, 31, and 33, patients who, though casting off large numbers of leucocytes in the sputum, show a normal Arneth picture. The extension of red bone marrow to the long bones was observed in the six necropsies in which examination was made, all of them on fatal cases of pulmonary tuberculosis. In these instances the marrow of the femur was found on histological examination, to be producing leucocytes.

In nontuberculous infectious disease the "shift to the left" is, as in tuberculosis, evidence of an excessive demand on the bone marrow, or, in other words, it is evidence that an excessive number of leucocytes are being destroyed. For example, in Case 16, lobar pneumonia, the demand for leucocytes is, naturally, excessive, since large numbers are required to combat the infection in the lung, and they are continuously being cast off in the sputum. In this instance the ratio of immature to mature cells reached 4.2. Cases 10 and 13, in contrast, illustrate the fact that although moderate toxemia may exist as shown by the leucocyte count and temperature, if polynuclear leucocytes are not attracted into the lesions in large numbers, the Arneth picture may remain normal. Case 17 is of especial interest. On March 3, 1915, the patient evidently had a septic pneumonia resulting from a postoperative embolism. At this time she showed clinical evidence of marked toxemia. The leucocyte count of 31,000 is evidence of a strong bone marrow reaction to the toxemia, and there is also a well marked "shift to the left" of the Arneth picture. Five days later, although the clinical condition was somewhat improved as a result of the evacuation of large quantities of pus by coughing, and although the white count had fallen to 16,000, the demand for leucocytes had apparently increased, and the "shift to the left" was more marked. On March 12, with an apparent extension of the abscess, the beginning of gangrene, a "septic temperature," and extreme prostration, the bone marrow reaction seemed poor, leucocyte count only 12,000, and the Arneth "shift to the left" was extreme. After operation on March 14, improvement in the general condition occurred, and on March 26, although the maxi-

mum temperature was only 100.6°, the "shift" in the blood picture was still extreme. This was probably because fairly large quantities of pus were still draining from the operative wound. The record for April 22 showed a marked clinical improvement and a return to normal of both the temperature and the Arneth picture, although the leucocyte count still remained elevated. This case appears to be a good illustration of the fact that leucocytosis is evidence of toxemia: i.e., toxic stimulation of the bone marrow; while on the other hand, the appearance of immature polynuclears, the "shift to the left," denotes excessive destruction and, therefore, excessive mobilization of leucocytes, and has no relation to toxemia.

In judging the value of the Arneth picture, it is necessary to keep in mind this conception of its meaning. In early tuberculosis of the lungs a "shift to the left" must mean necrosis and extension of the lesion, and therefore activity of the process. Here the study of the picture should prove of value. In Cases 45 and 46 such a "shift" was the earliest recognized sign of impending progression of the disease. In advanced pulmonary tuberculosis the extreme "shift" seen in the progressive cases is accompanied by such definite clinical evidence of activity that here its value is not great. When the disease is very slowly extending, as in chronic phthisis, there seems to be a marked variation in the picture as shown in Cases 31, 32, 33, and 34, without evident change in the clinical condition. Here also it is of little use. In nontuberculous disease, as the leftward "shift" indicates excessive mobilization and destruction of leucocytes, the study of the picture may be of use in determining the nature of an obscure infection, and in indicating the presence of large collections of pus. It seems certain that the Arneth picture cannot be considered an index of the resistance of the individual to infection.

SUMMARY AND CONCLUSION.

1. The presence of a high percentage of immature polynuclear leucocytes in the circulating blood (Arneth's "shift to the left") is evidence of excessive loss of polynuclear leucocytes from the blood stream, and an attempt on the part of the bone marrow to make good the loss.

2. It does not indicate toxemia, nor is it an index of the patient's resistance to infection.

3. Leucocytosis, on the other hand, is evidence of toxemia and of direct stimulation of the bone marrow by certain toxins. A moderate leucocytosis may exist without causing an appreciable change in the Arneth picture.

4. In pulmonary tuberculosis the demand for leucocytes indicated by a "shift to the left" means necrosis, and extension of the lesion. In early stages of the disease this may be of considerable value in immediate prognosis, and even, at times, in diagnosis. In advanced disease which is slowly progressing, as the demand for leucocytes apparently varies from time to time, the count appears to be useless in estimating the prognosis. In rapidly progressing tuberculosis the unmistakable clinical evidence of activity renders the study of the blood picture superfluous.

5. In nontuberculous disease the evidence of excessive mobilization of leucocytes may be of value in doubtful cases to determine the presence of large collections of pus.

A SIMPLE METHOD OF PLOTTING CHARTS*

By John R. Williams, M.D., Rochester, N. Y.

WITH the advent of precise methods of investigation in the medical sciences, the use of the graph as a means of conveying comparative mathematical information has become more and more common. The reason for this is very obvious. The graph, when properly arranged, shows at a glance what tables of figures will reveal only after long and patient study. Moreover, the relationship of one set of data to another and the general perspective of a study amenable to mathematical treatment can better be comprehended when plotted as a line drawing than when buried in a maze of tabulations.

One serious difficulty in the way of preparing graphs for hospital and laboratory use is that it requires the services of some one especially trained in this kind of work and such individuals are rarely to be found in the personnel of scientific institutions. Moreover, the labor of preparing graphic charts as ordinarily done, both as to time and expense, is prohibitive except in extraordinary instances.

In the writer's hospital service, where a number of diabetics and nephritics are under observation, it has been found desirable, both for purposes of study and teaching, to employ charts. For the above mentioned reasons, it has been impracticable to employ a draughtsman for routine work. The necessities of the situation, therefore, led to the development of the following method which answers the important requirements of most workers. A very elaborate chart can be made in an hour or two by an office assistant which, if drawn by a daughtsman in the usual manner, would take from one to two days. The materials are inexpensive; the printing and hatching are uniform; colors can be used in place of cross hatching when desired.

After much experimentation, a cross section paper was selected which may be purchased in sheets measuring sixteen by twenty-one inches. The bold ruling on this paper forms inch squares and the fine ruling one-tenth squares. A paper ruled to form half inch squares with the fine lines ten to the inch would be much better but this is not to be had, accordingly we have had the sheets reruled so as to have the bold lines one-half inch apart. A blank chart was then prepared containing all the words and figures which would appear on every chart. (See Fig. 1.) Blank spaces were left so that syllables, words, or numbers could be added as desired. On another sheet of paper, were drawn all the words and figures appropriately sized and spaced, which one might wish to add to a chart. These were so arranged that they could readily be cut out as needed. On another sheet were drawn eight different types of cross hatching, each one-half inch wide and of lines of sufficient boldness as to permit reduction for reproduction. (See Figs. 2 and 3.) From each of these, zinc etch-

*In the development of this method of plotting, I wish to acknowledge valuable aid and advice of Mr. Frederick W. Fisher and Mr. F. A. Miller of the Engineering Department of the Rochester Railway and Light Company and Mr. C. W. Norwood, draughtsman.

ings and electros were made. From the large electro, the charts were printed. The other two electros containing the miscellaneous words and numbers and the cross hatching were printed on white gummed paper.

When it is desired to prepare a chart, figures are cut out of the gummed sheet to make the patient's case number and pasted in the proper place. If the patient is a female, the syllable "fe" is prefixed to male, likewise the words "mild," and "severe" may be placed before the word diabetes to indicate the

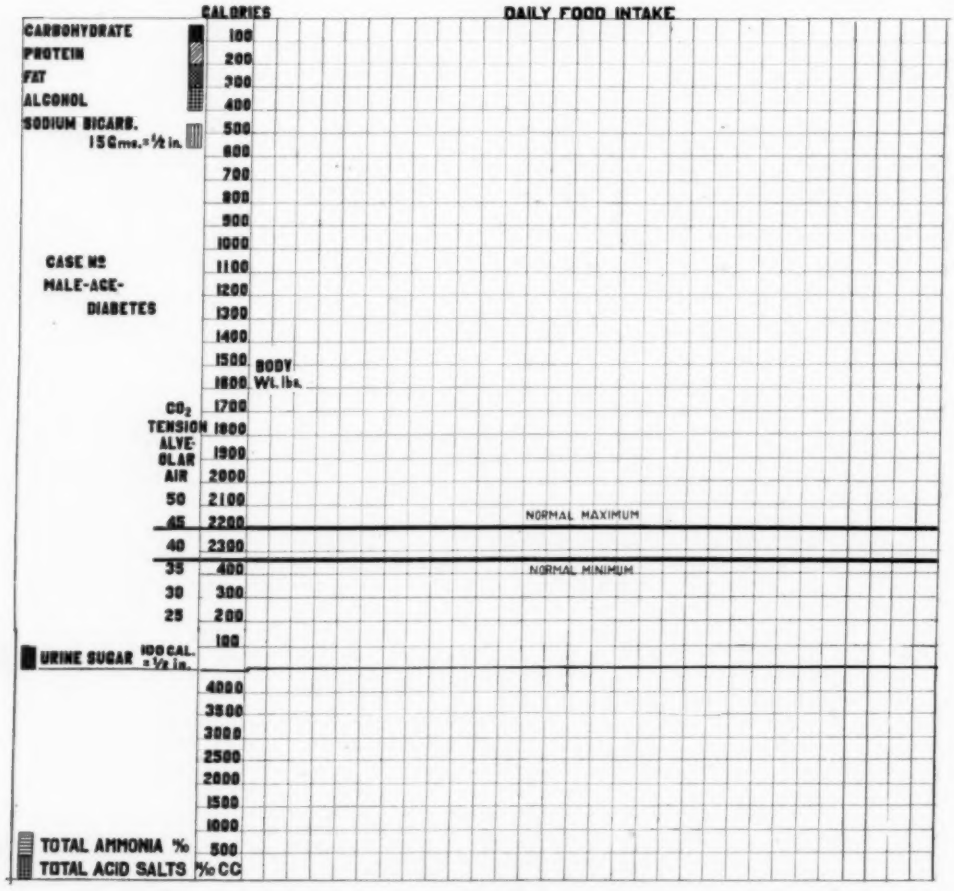


Fig. 1.—Blank chart used for plotting the metabolism of a case of diabetes mellitus.

severity of the case and the words "fatal" or "improved" to indicate its outcome. The date line is similarly added, the numbers being so spaced and sized as to fit each column which may represent a day of observation. The cross hatching is cut into strips and then into lengths to represent the quantities desired and these pasted in their appropriate columns. See finished chart, Fig. 4.

All of the trimming and cutting is done with a small inexpensive photographer's trimming board. To facilitate computations and reduce error to the minimum, a scale was prepared and attached to the trimming board which reads in grams but measures in calories. The scale has a double row of divi-

sions. The upper one is plotted for carbohydrates and proteins which have the same caloric value, one gram of either being equivalent to four and one-fourth calories. The lower line of divisions of the scale is arranged similarly for the fats, a gram of which is equivalent to nine calories. Accordingly, if one wished to plot the diet of a patient for several days, he would take from the hospital record the number of grams of carbohydrates, proteins and fats eaten each day. A piece of the cross hatching paper intended to represent carbohydrates would be placed on the cutting board at the figure representing the number of grams eaten and then cut. This piece, when moistened and stuck in its proper

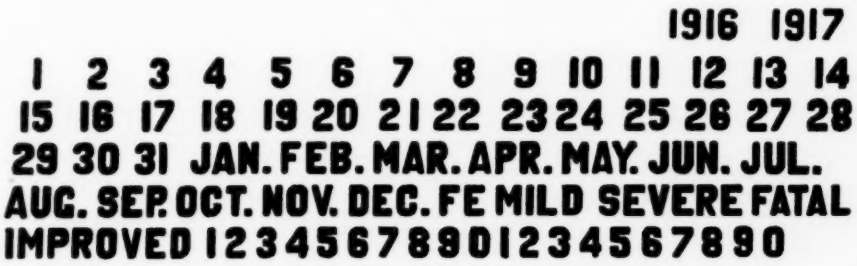


Fig. 2.—Words and numbers used in plotting a case of diabetes mellitus printed on gummed paper to be cut out and pasted on chart as needed.

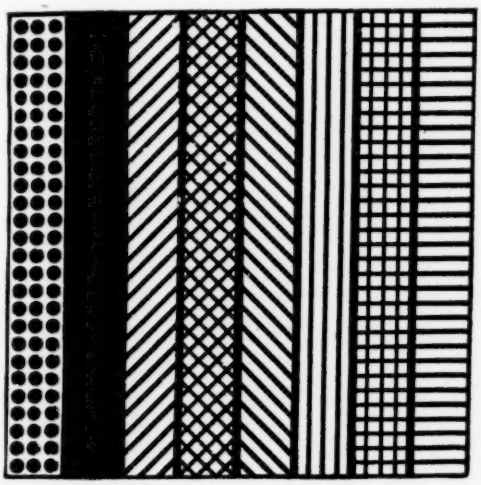


Fig. 3.—Eight types of cross hatching printed on gummed paper to be cut up and pasted on blank chart as needed. A simple way of avoiding the labor of draughting.

place on the chart, would then represent in length the number of calories in the number of grams of carbohydrate in question. The worker would be spared the labor of computation and the chance for error would be reduced to the minimum. Similarly, proteins and fats may be calculated and plotted. The total length of the cross hatching would thus represent the total number of calories. In the plotting of diabetic charts, the urine sugar is also plotted in calories so that the balance between intake and outgo may be seen at a glance. The weight line and curve of carbon dioxide tension of alveolar air are inked in with a ruling pen very quickly.

The accompanying figures illustrate the application of the idea to the plotting of the metabolism of diabetes; the method, however, lends itself readily to many other diseases, particularly nephritis, where it may be desirable to graphically compare the nonprotein elements of the blood with those in the urine and the relation of salt and food metabolism thereto.

The expense of preparation for making the charts was comparatively small, approximating fifteen dollars for one hundred charts, sixteen by twenty-one inches each. Thus the materials required to produce the chart shown in Fig.

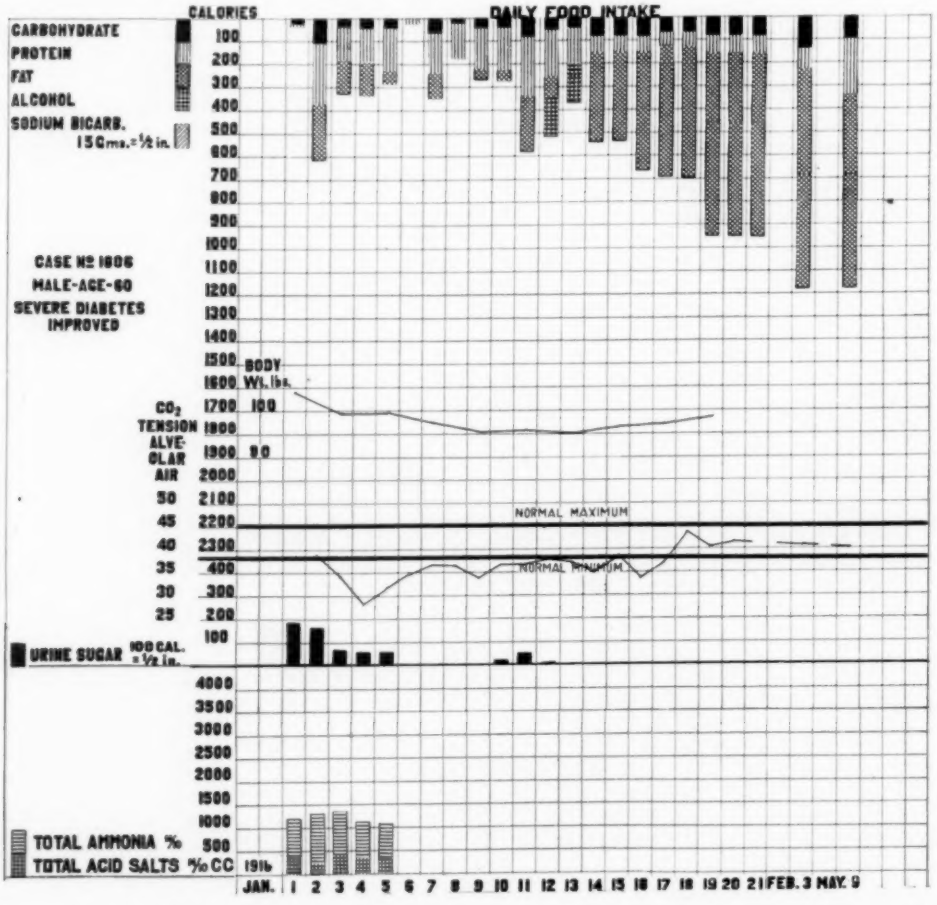


Fig. 4.—Showing practical application of the chart to a case of severe diabetes of long standing. This patient was excreting sugar and was in a state of marked acidosis although taking very little food. When the protein intake was reduced the patient immediately began to improve and in a short time was able to eat much more food than formerly with the same protein intake which before had caused injury.

6 cost approximately fifteen cents plus the labor of an assistant for about two hours.

The salient features of the method are:

1. The printing on standard sheets of cross section paper all the fixed words and characters which will be common to all charts. This usually can best be done by having them first drafted, and zinc etchings and plates or electros made therefrom.

2. The printing on gummed paper of all the common words and characters which the plotting of a given set of data will require. These to be of the proper size and spacing to fit in the chart so as to give uniformity.

3. The printing of several types of cross hatching on gummed stock so that it may be similarly used.

4. The use of a photographic trimming board to smoothly and correctly cut the words, characters, and hatching used and the attachment thereto of a scale to facilitate calculations and to minimize errors.

5. The facility and wide application of the method and its relatively slight cost.

MACROPHAGES IN FECES IN ACUTE DYSENTERY*

By Kenneth M. Lynch, M.D., Charleston, S. C.

IN the early part of 1916 my attention was called to several cases of acute dysentery in the Roper Hospital, of Charleston. A fairly typical example of these is the following case.

J. M. R., white male, age 20 years, mechanic, was admitted on Jan. 10, 1916. His previous history was negative of any connection with the present illness. He had had no similar attack. About midnight of January 4th he had developed a severe diarrhea accompanied by pain throughout the abdomen. This condition had become worse and he was passing twelve to fifteen stools a day before admission, at first of a watery character but later becoming mucinous and bloody. He said he had a good appetite, but when he ate anything, it would pass through directly. His tongue was coated and furred and of yellowish brown appearance. His abdomen was generally tender on palpation. His temperature was slightly subnormal in the morning and averaged a degree and a half rise in the evening. There was no sign of any involvement outside the alimentary canal.

With no treatment besides rest in bed and the administration of bismuth subnitrate by mouth he improved rapidly, the abdominal tenderness decreased, the pain disappeared, the number of stools decreased to two a day, his temperature remained normal or slightly subnormal, and he was discharged on January 15th.

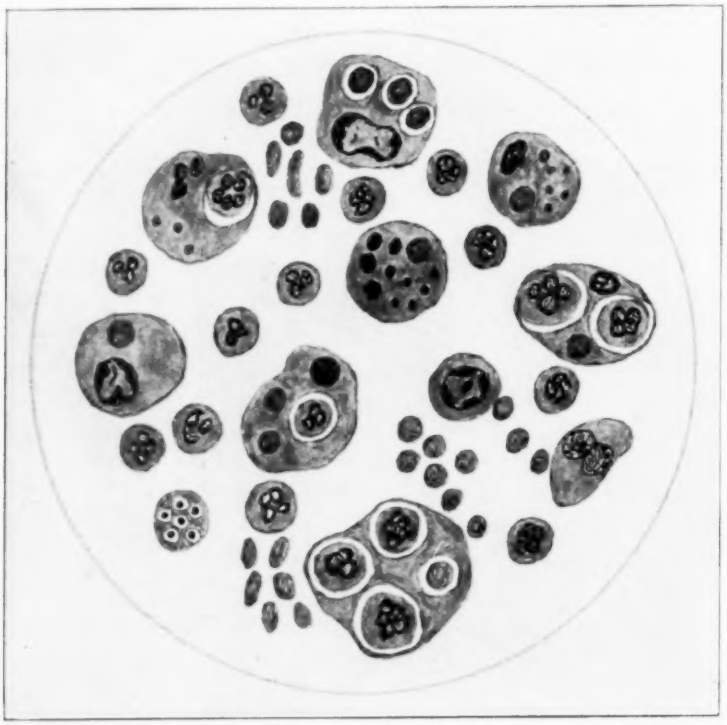
The first stool examined was of the appearance of thick blood-stained mucus. In a fresh warm wet preparation there were large numbers of polynuclear leucocytes and red blood cells, many active Trichomonas and an occasional Entamœba coli. In addition there was a considerable number of round or ovoid cells, varying in size from twenty-five to forty-five microns, nonmotile, with densely granular cytoplasm, and a large ring-form nucleus. The nucleus usually had a definite refractive membrane and from one to four refractive granules clinging to its inner surface or free in the plasma. In some of the cells there were two of these nuclei, some had apparently no nucleus and in some

*From the Department of Pathology and Research Medicine of the Medical College of the State of South Carolina.

it appeared to be represented by a group of large refractive granules without a limiting membrane.

Many of these large cells contained from one to three or four erythrocytes, and as commonly, from one to three polynuclear leucocytes, some containing both, usually within distinct vacuoles. Some of these engulfed erythrocytes were decreased in size and in some of the cells small bodies of the appearance of erythrocytes were seen. The engulfed leucocytes were commonly of the same appearance as the extracellular, but in many of the cells were refractive particles which were judged to be remnants of leucocytic nuclei.

Preparations stained by Heidenhain's iron-hematoxylon and by Leishman's methods confirm the observations made on the unstained specimens. In the



Macrophages in feces in acute dysentery. Case of J. M. R., Jan. 12, 1916. Heidenhain iron-hematoxylon stain.

stained specimens the broken up as well as the preserved red blood cells and leucocytes are of the same staining properties as those outside. Stained with hematoxylon the cytoplasm, and nucleus of the phagocytes are of the same color as in the leucocyte; but with Leishman's stain, the cytoplasm is blue and the nucleus purple.

While in the fresh preparation few bacteria were observed, in stained specimens they were fairly numerous, mainly engulfed by leucocytes. The predominant organism was a micrococcus.

The stool remained of bloody mucinous character for two days after admission; then as the number diminished, it gradually assumed the normal appearance,

the bacterial flora assumed the common proportions, and the cells gradually decreased in number until there were only a few leucocytes present. None of the large phagocytes was to be found after the second day, they disappearing before the red blood cells or leucocytes. The Trichomonas and Entamœba coli remained in small numbers.

Based on the lack of active motility, the character of nucleus, the staining characteristics, and the early disappearance from the stool, this large phagocytic cell was judged to be a large wandering body cell similar in nature to Mallory's endothelial leucocytes. While these so-called endothelial phagocytes are known to play an important part in phagocytosis within certain organs and have been reported to exhibit activity in serous cavities and even within the blood stream, their entrance in numbers into the intestinal canal apparently through a more or less intact mucosa appears to be an occurrence of interest, from the standpoint of the study of this cell, and also in microscopic study of dysenteric feces.

Although a close study cannot fail to differentiate them, the occurrence of such phagocytes in a dysenteric stool of this character might easily lead to confusion with Entamœba by the uninitiated.

While no definite determination as to the cause of the enteritis in these cases was made, I considered it as probably bacterial and possibly the micrococcus which was the predominant organism in the stool and extensively phagocytized by leucocytes.

A FURTHER STUDY OF THE PATHOLOGICAL EFFECTS OF ATMOSPHERES RICH IN OXYGEN*

By Howard T. Karsner, M.D., Cleveland, Ohio, and J. Earle Ash, M.D., U. S. Army.

A PREVIOUS study† showed that in the case of the rabbit "atmospheres containing 80 to 90 per cent oxygen under normal barometric pressure produce in 24 hours, or more commonly 48 hours, congestion, edema, epithelial degeneration and desquamation, fibrin formation, and finally a pneumonia probably of irritative origin and to be described as fibrinous bronchopneumonia." The present study deals with a series of animals exposed to atmospheres containing 53 to 80 per cent oxygen. The purpose of the study is to determine whether or not these lower percentages operate to produce lung changes as rapidly or in the same degree as do the higher percentages previously reported. The apparatus, care of animals, use of contemporaneous controls, and pathological technic were the same as in the earlier work.

One rabbit was placed in the chamber with an atmosphere containing 53 per cent oxygen for 3 days, 16½ hours. A control was placed in the same sized cage with room air. Both animals were removed alive and apparently well. The autopsies showed no pathological alteration of lungs or other viscera.

Two rabbits were placed in the chamber with about 67 per cent oxygen for 3 days, 18½ hours. The usual control was employed. The animals were removed alive and apparently well. The lungs of the animals exposed to "high" oxygen showed moderate congestion associated with slight cloudy swelling of alveolar epithelial cells; there was neither desquamation nor exudation.

Three rabbits were placed in the chamber and stayed 11 days during most of which time the oxygen percentage varied between 60 and 70. For a few hours on the first day and again on the fifth day the oxygen content sank to normal; on the second day the oxygen rose for a very short period to 78 per cent. The animals were removed at the end of 11 days alive and apparently well. In the case of one of these animals, the lungs were perfectly normal except for a slight congestion, not more marked than in the normal control. Another animal showed marked congestion of the lungs with a small amount of edema within the alveoli as well as slight congestion of the abdominal viscera, not more marked than in the control. The third animal showed moderate swelling of the alveolar epithelium and a few alveoli showed desquamation of the swollen cells; there was, however, no fibrin formation, edema, or exudation. The abdominal viscera of all three animals showed slight congestion but not in greater degree than in the control.

Two rabbits were placed in the chamber with oxygen content of about 75 per cent. On the third and fourth days, however, the oxygen rose for a few hours to 90 per cent. They were then kept in room air for 4 days. Following

*From the Nutrition Laboratory of the Carnegie Institution of Washington, Boston, and the Laboratories of Pathology of the School of Medicine of Western Reserve University, Cleveland, and the Harvard Medical School, Boston.

†Karsner, H. T.: The Pathological Effects of Atmospheres Rich in Oxygen, Jour. Exper. Med., 1916, xxii, 149.

this they were placed in the chamber for 6 days with 74 per cent to 78 per cent oxygen, at the end of which time they were found dead. Both animals showed well marked pneumonia, cloudy swelling of the myocardium and marked congestion of the abdominal viscera.

Two rabbits were placed in the chamber with oxygen averaging about 75 per cent for 10 days. On the seventh day the oxygen sank to 44 per cent for a short time and later rose for a short time to 91 per cent. The animals were removed on the eleventh day, alive but weak and dyspneic. The lungs of these animals showed slight congestion but not in greater degree than in the control. The abdominal viscera showed well marked congestion.

It is apparent that a short exposure (3 days, 16½ hours) to 53 per cent oxygen produced no apparent change in the rabbit's lung. Exposure to 67 per cent oxygen for a short period (3 days, 18½ hours) produced extremely slight changes, so slight as to be distinguished only after most careful examination. Three rabbits exposed for 11 days to atmospheres between 60 per cent and 70 per cent oxygen showed very slight evidences of pulmonary irritation but no true inflammatory reaction. Exposure for 10 days to 75 per cent oxygen showed an early pneumonia. The same was true of 2 additional animals exposed to approximately the same atmosphere for 6 days but complicated by accidental exposure to air of a higher percentage (90 per cent) 4 days before the last experimental period.

It will be seen that there is considerable difficulty in maintaining a constant oxygen percentage in the chamber during the long periods demanded in this series. On the other hand, departures from the desired constant were of brief duration and with the exception of one pair of animals apparently of no importance in the outcome of the experiment.

This study confirms the earlier study in regard to the inter-relationship of pneumonia, myocardial cloudy swelling, and the congestion of the abdominal viscera. It is shown that animals exposed to atmospheres containing less than 80 per cent oxygen and more than 60 per cent oxygen withstand the exposure for a considerably longer period than those animals exposed to percentages greater than 80 per cent. This must not be interpreted as indicating that 80 per cent is a critical point in the scale of percentages. Reference to the previous paper will show that this point was selected merely as a matter of convenience.

The correlation of this study with its predecessor will indicate that in a very broad general way, and modified probably in many ways by uncontrollable factors in the individual animals, the higher the percentage of oxygen in the atmosphere, the earlier do pneumonia and the secondary changes in the other organs make their appearance.

BLOOD PRESSURE IN THE AGED

A Study of 150 Cases from 65 to 95 Years of Age.

By L. M. Bowes, M.D., Chicago.

A GREAT deal of work is being done, in the study of blood pressure, at the present time. It is of special interest in the aged because so many of the diseases have characteristic findings, and it aids us, not only in differential diagnoses, but also in prognoses and treatment. It is because of this aid that I have made a study of these cases.

On account of the different methods and positions of taking blood pressure, I am giving a brief description of the technic which was employed in this work.

The patient was seated in a chair with the bared left arm partially flexed, supinated and resting on a table. The armlet was then applied to the arm on a level with the heart and adjusted to be read conveniently and quickly. The bell of the stethoscope was applied just below the flexure of the elbow and a little to the inner side. The armlet was then gradually inflated until a point 10 mm. Hg. above that at which all sound disappeared had been reached. The air was then allowed to escape, slowly, noting the point when the first sound appeared. The air was allowed to escape further until the pressure dropped from the point of maximum intensity to a dull tone. This point was recorded as the diastolic pressure. The difference between these readings was recorded as the pulse pressure.

On account of the great hardness of the blood vessels of some patients, it was very difficult to get a true and accurate reading, making it necessary to make repeated observations to correct or verify former findings. The artery below the flexure of the elbow of one patient was misplaced so that the reading could not be made by auscultation. This case is not included in this series.

In some patients who were apprehensive it was necessary to adjust the armlet for a little while before taking the blood pressure, and wait until they became accustomed to the procedure and relaxed sufficiently to make an accurate reading. When the patient became nervous, the systolic pressure was almost invariably raised 10 to 25 mm. Hg. When the observations were made too frequently the systolic pressure was often increased 5 to 10 mm. Hg. probably due to spasm of the vessel wall. As a large number of the aged tire easily, the readings were made as quickly as possible. It was noted that when they became tired during the observations, the systolic pressure fell 5 to 10 mm. Hg.

In one case the pressure in the armlet was maintained a little too long causing one of the small vessels in the anterior portion of the wrist to rupture, resulting in a slight hemorrhage extending over an area about four inches in length. The discoloration cleared up in about a week with no bad effects. The air must be entirely released between each separate reading and not maintained too long.

Seventy-five per cent showed an inequality of the blood pressure on the two sides of the body. Where this condition was constant, the arteries were always quite sclerosed. Of seventy-five per cent of those showing a difference of blood pressure in the two arms, an inequality was shown in the systolic pressure, and

sixty per cent in the diastolic pressure. There was an inequality of the diastolic pressures in only one instance where the systolic pressures were equal. Where there was an inequality of the systolic and diastolic pressures, seventy-five per cent were higher in the left arm.

The greatest difference shown was a man, aged 74, who complained of dizziness. He had a combined aortic and mitral regurgitation. The arteries were greatly sclerosed. The pulse was 50. On the left side the systolic pressure was 178, the diastolic pressure 104, and the pulse pressure 74 mm. Hg. On the right side the systolic pressure was 230, the diastolic pressure 104, and the pulse pressure 126 mm. Hg.

Engel believes that this sign may be useful in differentiating between primary nephritis and arteriosclerosis. The only instance in which I found this inequality in nephritis, was a man, aged 70, who complained of swelling of the limbs and pain in the back. The heart was normal and the arteries slightly sclerosed. The systolic pressure on the left side was 232, the diastolic pressure 115 and the pulse pressure 117 mm. Hg. On the right side the systolic pressure 190, the diastolic pressure 112 and the pulse pressure 78 mm. Hg. The urine was acid and the specific gravity 1030. Both albumin and sugar were present.

A man, aged 75, whose right leg was amputated at the junction of the upper and middle thirds, because of septic arthritis, had a systolic pressure of 142, a diastolic pressure of 85, and a pulse pressure of 57, on the left side, and a systolic pressure of 120, a diastolic pressure of 65 and a pulse pressure of 55 mm. Hg. on the right side.

In a case of senile dementia the blood pressure was equal. The patient was a woman, aged 67, with a normal heart. The arteries were greatly sclerosed. The systolic pressure was 144, the diastolic pressure 72, and the pulse pressure was 72 mm. Hg.

There were 100 women and 50 men examined in this series. The systolic and pulse pressures increased to the age of 85 and then decreased. The diastolic pressure did not vary much after the age of 70 (see Table I).

The blood pressure was higher in women except after the age of 90 (see Tables II and III).

TABLE I.—THE AVERAGE BLOOD PRESSURE OF BOTH MEN AND WOMEN.

Age.	Number examined.	Systolic pressure.	Diastolic pressure.	Pulse pressure.
65-69	32	151	82	65
70-74	39	160	86	73
75-79	38	166	86	79
80-84	27	175	84	83
85-89	7	170	90	77
90-94	7	142	81	61

TABLE II.—THE AVERAGE BLOOD PRESSURE OF THE WOMEN.

Age.	Number examined.	Systolic pressure.	Diastolic pressure.	Pulse pressure.
65-69	21	154	83	71
70-74	29	158	83	72
75-79	24	170	88	81
80-84	16	183	85	91
85-89	7	170	90	77
90-94	3	137	80	53

TABLE III.—THE AVERAGE BLOOD PRESSURE OF THE MEN.

Age.	Number examined.	Systolic pressure.	Diastolic pressure.	Pulse pressure.
65-69	11	145	81	63
70-74	10	166	91	75
75-79	14	159	89	77
80-84	11	163	84	80
85-89	0	—	—	—
90-94	4	145	81	65

There were a few who had very high blood pressure without symptoms. They were going about their every-day duties in apparently perfect health.

There were some who simply complained of a morning headache, slight vertigo, numbness or tingling of the hands and feet.

A third group presented the more severe symptoms of nephritis, aortic regurgitation, cerebral hemorrhage, and arteriosclerosis.

There were 22 who had systolic pressures of 200 mm. Hg. or over. Thirteen had arteriosclerosis alone, 3 had cardiac lesions, 2 had nephritis, 2 had cerebral hemorrhage and cardiac lesions, 1 cerebral hemorrhage, and 1 nephritis and a cardiac lesion. The highest systolic pressure was 270 mm. Hg. This was a case of nephritis.

There were 28 who gave diastolic pressures of 100 or over. Sixteen had arteriosclerosis alone. Seven had cardiac lesions, 2 had cerebral hemorrhage and a cardiac lesion, 2 cardiac lesions and nephritis, and 1 had cerebral hemorrhage.

There were 30 who had pulse pressures of 100 or over. The highest pulse pressure was 150, observed in a case of aortic regurgitation. Sixteen had cardiac lesions, 7 arteriosclerosis alone, 3 cerebral hemorrhage, 3 nephritis, and 1 had nephritis and a cardiac lesion.

All cases of nephritis had very high blood pressures. Where there was a continuous hypertension, nephritis was present, or the findings of chronic interstitial nephritis presented themselves in the majority of cases. Those escaping were the subjects of cerebral hemorrhage.

The blood pressure was of no practical value in any of the heart lesions except aortic regurgitation. In these cases the pulse pressure was always very high due to the low diastolic pressure or both high systolic and low diastolic pressures. The following case is an illustration. The patient was a woman, aged 77, who had a compensated aortic regurgitation. The systolic pressure was 214, the diastolic pressure was 75, and the pulse pressure was 139 mm. Hg.

Where there was a combined nephritis and organic heart disease, the blood pressure was very high. In these cases of hypertension the heart had hypertrophied sufficiently to maintain the tension.

Where there was broken compensation accompanied by rapid and irregular heart action, the tincture of digitalis was used with good results. I have never seen injurious results follow its careful use in cases of broken compensation.

The systolic, diastolic, and pulse pressures were high in all cases of cerebral hemorrhages. In all cases of very high blood pressure, especially diastolic, after heart and kidney lesions were eliminated, the proper precautions were carried out to safe-guard against hemorrhage. The pressure dropped slightly following hemorrhage, but not permanently.

In one woman, aged 80, who is not included in this series of cases, the hemorrhage was from the eyeball. A year later there was a rupture of the other eyeball with hemorrhage. Infection and then meningitis followed.

Some of those with the hardest arteries presented normal blood pressure and appeared in good health. Some with normal radial arteries had hypertension. Only about 25 to 30 per cent with marked arteriosclerosis presented high blood pressure. A high pulse pressure was common.

Acute enteritis caused a fall of 5 to 15 mm. Hg. The blood pressure was low in cases of myocarditis, failing heart, and cerebral embolism. The latter fact may be of value in differentiating between cerebral hemorrhage and cerebral embolism.

The blood pressure may be low and still present no indication. A man, aged 65, who was attending his business every day had a systolic pressure of 100, a diastolic pressure of 60 and a pulse pressure of 40 mm. Hg.

A low pulse pressure was associated with myocarditis or a failing heart; and a sustained pulse pressure of 100 or over usually resulted in myocarditis or a failing heart.

In most cases of bronchitis there was a failing heart with lowering blood pressure. One woman, aged 81, had hypertension.

There were four cases of carcinoma, three of which had normal blood pressure. Two had involvement of the right breast, and one, the nose. The fourth case was a woman, aged 79, who had a carcinoma of the stomach with the characteristic coffee ground vomitus. The systolic pressure was 232, the diastolic pressure 130, and the pulse pressure was 102 mm. Hg.

Obesity did not seem to influence the blood pressure, as one woman, aged 76, who weighed about 270 pounds, had a systolic pressure of 160, a diastolic pressure of 80, and a pulse of 80 mm. Hg.

CONCLUSIONS.

1. Only repeated readings of both systolic and diastolic pressures are of value, and both arms should be used for observations in old people.

2. Inequality of the pressures of the two sides is frequent in arteriosclerosis.

3. There may be a high or low blood pressure in arteriosclerosis; the pressure falling with involvement of the heart muscle in the process of fibrosis resulting in chronic myocarditis.

4. High systolic pressure associated with high diastolic pressure indicates cerebral hemorrhage or nephritis.

5. A sustained hypertension, both of systolic and diastolic pressures, indicates cerebral hemorrhage, while hypotension indicates cerebral embolism.

6. A sustained high systolic with a low diastolic pressure usually indicates cardiac trouble. A low diastolic pressure is common with aortic regurgitation.

7. A high pulse pressure is frequent in arteriosclerosis and aortic regurgitation; and a sustained high pulse pressure usually results in a failing heart.

8. A systolic pressure of 100 may not keep a man from his daily business.

9. A lowering blood pressure indicates a failing heart.

10. Acute enteritis lowers the blood pressure.

LABORATORY METHODS

THE DEMONSTRATION OF TREPONEMA PALLIDUM IN THE CEREBRAL CORTEX OF A CONGENITAL SYPHILITIC CHILD*

By Charles E. Kiely, M.D., Cincinnati, Ohio.

THE following report has to do with the demonstration of the T. pallidum, by means of the Noguchi technic, in the central nervous system of a syphilitic child.

The clinical history is as follows, and for it I am indebted to the Pediatric Service of the Cincinnati General Hospital. The child (Hospital No. A-5469) was admitted to the hospital on August 13, 1916, suffering from a discharging sinus in the back. The family history was not obtained.

Past History.—The patient was born three days before admission and at the time of birth showed a tumor over the lower part of the spine, extending about two inches along the spinal column and containing a clear liquid covered by only a very thin membrane. This tumor was about six inches long and four wide. The tumor already showed signs of sloughing. Otherwise the child seemed normal.

August 20, 1916.—The patient had a purulent discharge from the back and the tumor had disappeared.

August 30, 1916.—Patient showed evidences of meningitis with bulging fontanelles and rigidity of the muscles of the back; and a subnormal temperature.

September 10, 1916, Patient died.

Clinical Diagnosis.—Spina bifida; meningitis.

Autopsy Protocol (M.)—The body was that of a white female child about 18 inches in length. Postmortem rigidity had disappeared and lividity was present. There was an over-riding of the bones of the skull. There were no teeth present in the mouth. Upon each heel there was an area measuring 3 cm. in diameter, which appeared to be an ulceration due to pressure.

Over the lumbar region there was a reddish ulceration that measured fully 5 cm. in diameter. Upon section through this, it was found that the dura mater of the cord presented itself immediately and the vessels of the dura and of the cord beneath were found to be inflamed. The dura was adherent to the under surface of the ulceration and to the spinal canal just adjacent, but did not protrude as an open wound.

No abnormality was found in the lungs, heart, spleen or kidneys. The liver was larger than usual, very dark red in color, soft, and on section the organ cut readily, the cut edge turning out and from it could be expressed a blood-tinged fluid.

On opening the skull the dura was not found to be unusually adherent. The brain was large and soft and on pressure there escaped from both lateral

*From the Pathologic Institute of the Cincinnati General Hospital.

ventricles fully 500 c.c. of a clear, straw-colored fluid. The inner lining of the lateral ventricles was smooth and atrophic in appearances.

Anatomic Diagnosis.—Spina bifida; meningitis of the cord; hydrocephalus; hereditary syphilis.

When received by the writer the brain was in 10% formalin. In addition to the notes made at the postmortem table it may be said that the ventricles

Fig. 1.—Gross photograph of the brain after hemisection in the coronal plane. The shell is decidedly thicker here than elsewhere as the section passes through the basal nuclei. The ventricles have been mechanically distended for photography.

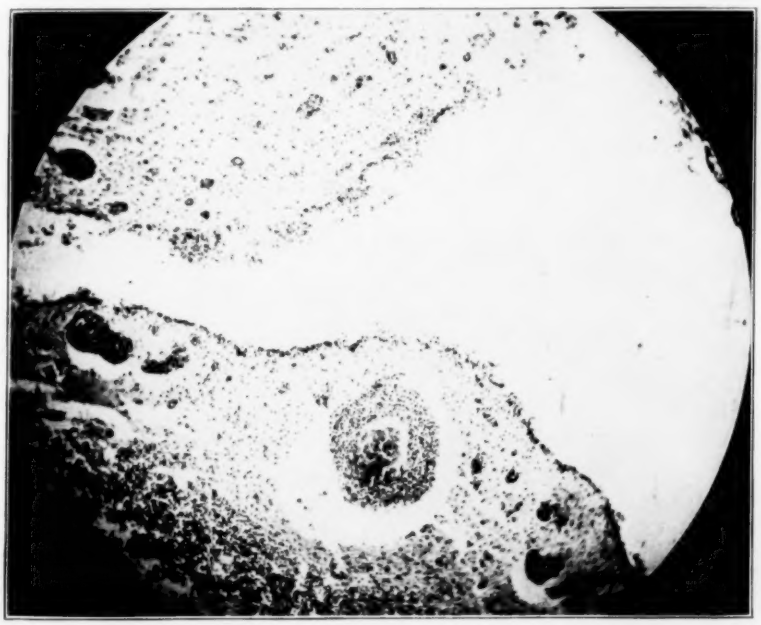


Fig. 2.—Section through the upper level of the pons. Microphotograph. The clear, roughly triangular area is the fourth ventricle.

were necessarily tremendously dilated and the substance reduced to a shell averaging about three-quarters of an inch (Fig. 1). The iter and the fourth ventricle were patent and not in the least distended. The choroid plexuses were reduced to mere fibrotic strands. The veins of Galen could not be recognized. Microscopically the plexuses are infiltrated with small round cells and

largely sclerotic (Fig. 3). The brain substance had a gelatinous feel and was extremely friable. Sections through the upper level of the pons showed a moderate thickening of the pia with small round cell infiltration. The reaction in the vessels was more marked; they were greatly engorged even to the fine capillary branches. The larger vessels showed a tremendous infiltration

Fig. 3.—Microphotograph of the choroid plexus.

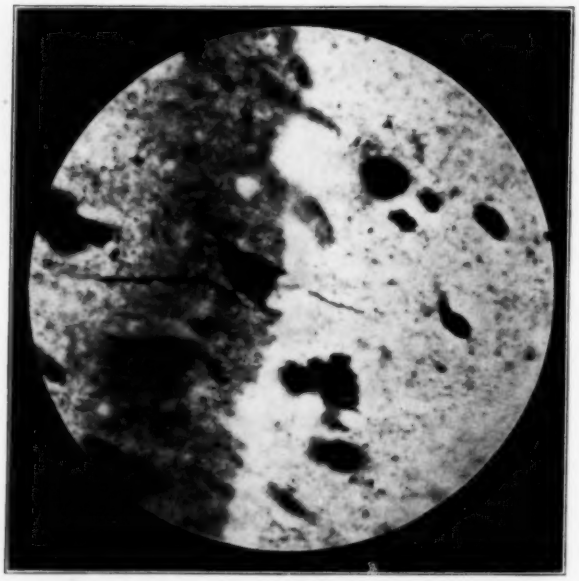


Fig. 4.—Noguchi preparation. Left of the nerve cell in the center of the field is a neuro-fibril. To the right is a treponema. Between this and the nerve cell is another treponema not in focus of this photograph but which to the eye was quite typical when in focus.

with small round cells (Fig. 2). The ependyma of the fourth ventricle was exfoliated to a considerable extent.

Sections through the entire thickness of the cortical shell were stained by the Noguchi technic. Treponemata were found with comparative ease and in rather large numbers considering their usual scarcity in nervous tissue. (Figs. 4 and 5.) These sections have been reviewed by Professors Wherry, Woolley, and Morris and the diagnosis sustained.

The mechanism of the hydrocephalus offers some difficulty. The lack of deformity in the iter and fourth ventricle preclude obstruction at the foramina of Luschka or Magendie. The iter was plainly patent. Experimentally hydrocephalus has often been produced by obstruction of the veins of Galen.[1] Such may have been the mechanism here. Transudation from the diseased vessels or tissues is a possible explanation and the one ascribed for such cases

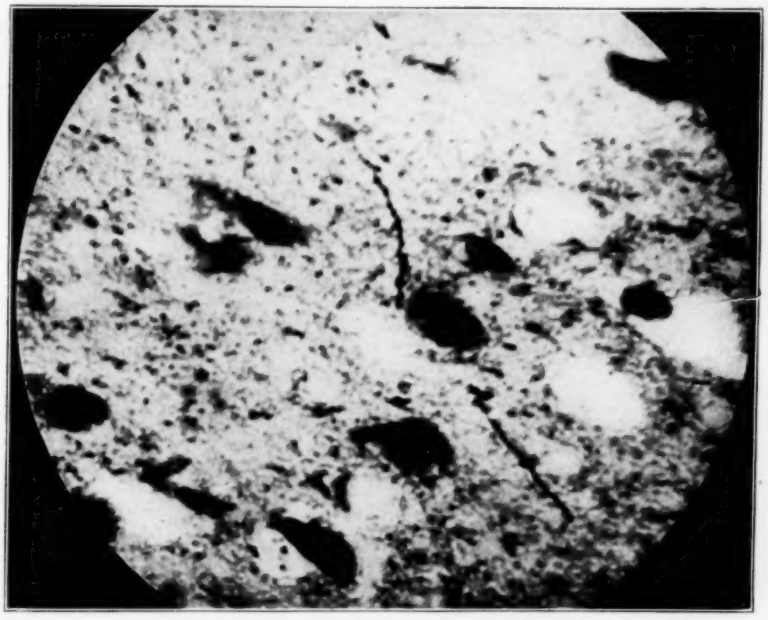


Fig. 5.—Noguchi preparation: a second field showing two treponemata.

by Nonne,[2] who says, "In many cases, a syphilitic arteritis is probably the cause of the hydrocephalus, and primarily also the cause of the congenital malformations produced by the hydrocephalus. The vessel disease promotes the exudation of lymphatic fluid in early intrauterine life, which causes a watery accumulation in the brain vesicles and the central canal."

The cord was unfortunately not secured in this case. There were no signs of acute meningitis in the portions of the central nervous system, i.e., the brain and brain stem which came into my hands. In the silver preparations there was no evidence of ependymitis.

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A MACHINE FOR SHAKING BLOOD-MIXING PIPETTES*

By Geo. G. Little, M.E., Rochester, Minn.

TO eliminate all shaking by hand of the glass tubes used to determine the number of red and white corpuscles to a cubic millimeter in testing blood, a motor-driven machine was designed and built to duplicate the hand method as nearly as possible.

Fig. 1.—*A*, cube.

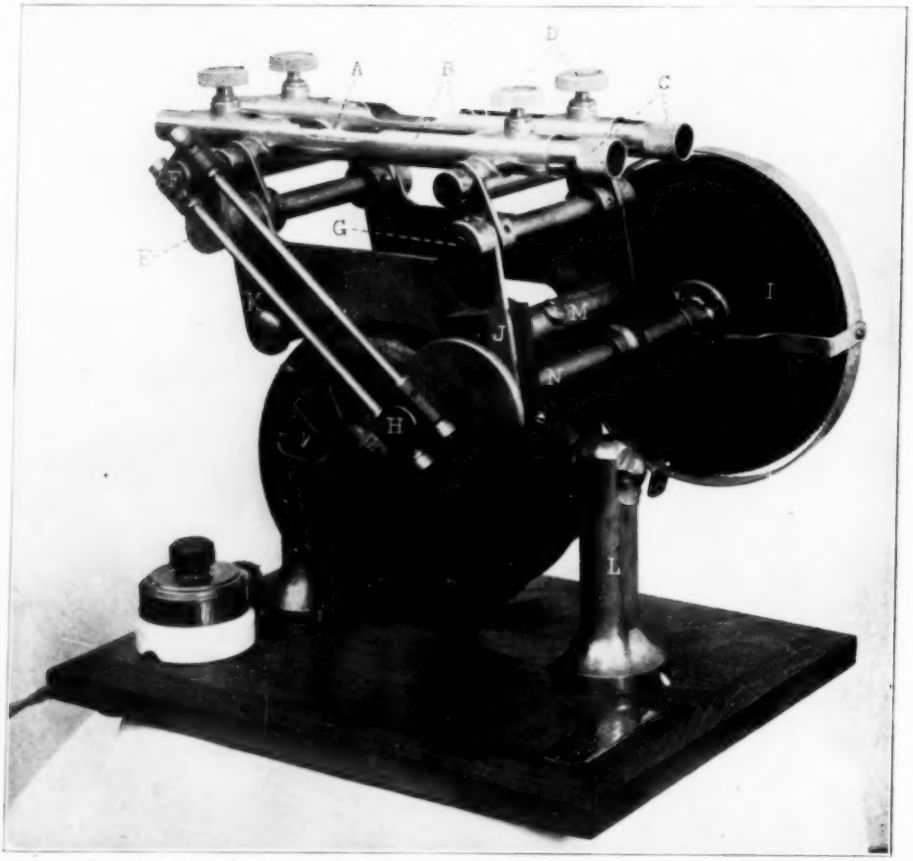

Fig. 2.—Machine for shaking blood-mixing pipettes. Baseboard 9x12 inches; height of instrument 9 inches.

*From the Instrument Department of the Mayo Clinic, Rochester, Minnesota.

A study of the hand motion while shaking the tube was made to determine the exact movement, the number of strokes per minute, the length of time per tube and the possible saving of time from the use of a machine.

The hand movement showed the tube to be moving through an arc the radius of which was equal to the distance from the tube to the wrist, and the length of the stroke to be about two inches.

Two tubes are usually shaken at one time by the hand method. They are held endwise between the thumb and the first and middle fingers and given a rapid reciprocating movement lengthwise.

A pipette or tube (Fig. 1) has a bulb or enlarged portion near the middle containing a small glass cube as shown at (*A*). This bulb is open to the air through a fine hole about one-tenth of a millimeter in diameter. Through it a solution is drawn and into the solution a few drops of blood. The tube is then shaken to throw the cube from side to side through the mixture. In this manner the blood corpuscles are separated so that when distributed in a measured thin layer on a glass slide they can be readily counted by the aid of a microscope.

Fig. 2 shows the machine mounted on a small fan-motor. An idea of size is given by the motor and the large gear both of which are about six inches in diameter.

The pipette (*A*) is shown in position ready to be shaken.

The holder (*B*) is made of brass tubing. Lugs are soldered in place to hold thumb screws (*D*) which serve to secure the adjustable slides (*C*) in place while the tubes are being shaken.

The inner ends of the slides (*C*) contain rubber tips which receive the ends of the pipettes, pressing against and closing the holes and thus keeping the solution from being shaken out of the tube.

The holders (*B*) are secured to cross trunnions bearing in the upper ends of the short arms on the shafts (*G* and *E*) and are moved through an arc. The radius of the arc is one inch and the stroke one and one-half inches.

The wrist (*F*)carries the upper end of the connecting rod which transmits the motion of the wrist (*H*) on the crank shaft (*N*) driven by the gear (*I*) which meshes directly with the pinion on the motor shaft.

The bearing blocks (*J*) are made of fiber and are secured to the side frame (*K*). They support the crank end of the shaft (*N*) and are split at the lower ends and fitted with screws to take up the wear of the shaft.

Two space rods (*M*) secure the side plates in position on the motor as well as hold them in alignment.

The motor is supported by two standards (*L*) which are secured to the base board and have lead washers underneath to deaden the slight noise of the motor and gears.

The board is nine by twelve inches and a snap switch for starting and stopping the machine makes it complete.

The installation of this machine saves the services of one assistant.

FURTHER NOTES ON A MODIFICATION OF THE NOGUCHI TEST*

By Norman E. Williamson, M.D., Stockton, Calif.

THE results of 142 tests by the short method advocated in a recent article follow:

CLINICAL DIAG.	AUTHOR'S MODIFICATION OF NOGUCHI.	NOGUCHI OR WASSERMANN.	NUMBER.
Negative	Negative	Negative	86
"	Negative		35
"	Negative	Weakly positive (+) Noguchi	1
"	Suspicious ±	Negative	5
Syphilitic	++	++	5
"	++		2
"	++	Negative	2
"	++	Suspicious ±	1
"	Suspicious ±	Negative	2
"	Suspicious ±	Suspicious ±	1
"	Negative	Negative	2

For Noguchi and Wassermann tests the serum was inactivated. Acetone insoluble fraction was used as antigen. Sach's antigen would have made a better showing, but positives must be checked by a less sensitive antigen.

Noguchi antigen can be used with cholesterin and makes an exceedingly sensitive antigen which can be used with active blood in my modification. It is not more hemolytic or anticomplementary than the antigen from which it is derived. I use 0.5 c.c. of 1% cholesterin in absolute ethyl alcohol added to 1 c.c. of the methyl alcohol solution of the acetone insoluble fraction. One part of this to 9 parts of salt solution makes the emulsion. I used 0.1 c.c. of this in 11 tests and had one positive (++) reaction that was negative by Noguchi antigen. This case gave a syphilitic history. I consider that negatives with this antigen have a decided value; positives require investigation.

I now use test tube racks with 4 rows of holes. I obtain 0.12 c.c. of blood from the ear and add it to 3.88 c.c. of the salt solution, containing 4 parts per 10,000 of sodium citrate, in a wide test tube. This facilitates shaking. One c.c. is added to each of the four tubes. In the front row Noguchi antigen with cholesterin is used; in the next Noguchi antigen; the third contains the anticomplementary control; the 4th contains nothing during the first incubation to determine fragility of cells; later 3 units of amboceptor are added, as in the other tubes, as a measure of human complement.

When such fresh blood was used I was unable to detect complementary action in 18 cases, in the presence of 1½ units of amboceptor. When 3 units are used there is a faint tinge of hemolysis in about 20% of the cases. If the tube with antigen shows no more color than the fourth tube, complete inhibition of the guinea pig complement can be recorded. So far I have not seen a case in which the human complement was a factor of any force.

*From the State Hospital, Stockton, California.

Tchernogubou used sodium citrate and utilized the human complement to hemolyze the patient's cells, as in this test. This cannot be an accurate gauge of the amount of complement fixed, and requires an enormous amount of amboceptor. The action of the sodium citrate on amboceptor seems to have been overlooked. This I will refer to again.

Von Dungern defibrinated blood, which of itself would produce some hemolysis. He used the patient's cells and disregarded human complement. He used an alcoholic extract as antigen which would give nonspecific proteotropic reactions. He used 0.1 c.c. of blood which is a large amount for active blood, and which would moreover occasionally contain an appreciable amount of complement.

I was convinced by my original experiments that sodium citrate did not affect the substance in syphilitic blood that was responsible in the presence of antigen for the complement fixation or absorption, and the results here tabulated show that this observation is correct. It was necessary to determine the action of the citrate on the other factors in the test. That cells are not affected has been shown by daily experience in obtaining them for complement fixation. Guinea pig serum 14 hours old was titrated as follows: to one portion was added 4 parts of salt solution; to another portion was added 2 parts of salt solution and two parts of 1% citrate salt solution. This makes about the proportion of citrate which would have been added to the whole blood to prevent clotting. There is this difference, however, that the calcium has been used in the clotting of the blood and the citrate is an excess. The two portions of 20% complement were titrated in parallel rows in the usual way with 1 unit of amboceptor and 1 c.c. of 1% suspension of washed human cells; 0.01 c.c. was the interval between tubes. The salt solution complement showed a unit of 0.08 c.c. The citrated complement reached maximum hemolysis at the same point, the hemolysis being almost, but not quite, complete. There were just a few more cells in the tubes containing more complement. This showed that there was no effect on the complement, but did suggest a deleterious action on amboceptor.

Fresh guinea pig blood was added to an equal quantity of 1% sodium citrate, centrifugated, and decanted. It was at once tested for complement. It was present but not strong. The next day the complement was strong. Just enough 1% calcium chloride was then added to a portion to produce clotting. On separation of the clot the complement was found to be unaffected. Calcium chloride in excess of this amount was anticomplementary, as is known. It may be possible that excess of calcium is one of the factors concerned in the anticomplementary action of some sera. None of the bloods used in the test in question have appeared to have a marked anticomplementary action. This may, however, be due to the freshness of the material.

Adding measured amounts of 1% sodium citrate in making the dilution of amboceptor it was found that one unit of amboceptor was destroyed by 0.2 c.c. of 1% citrate salt solution. That this was not caused by change in osmotic tension was shown by adding salt solution in the same concentration. It took 0.5 c.c. to have the slightest detrimental effect on the reaction. The citrate used in the test has united with calcium and very little is free. The extra unit of amboceptor

found to be of advantage in this test is to overcome the antihemolysin present in many bloods for the patient's own cells; to produce a quick reaction for early reading; to anticipate by such early reading the strengthening of the human complement. I believe, moreover, it assists in eliminating false positions. Patients showing suspicious reactions should be made the subject of thorough investigation. Five out of seven were shown by careful study, including examination of spinal fluid, to be in all probability free from syphilis.

After the tubes have stood for many hours a clot forms in each tube. This suggests the possibility of a chemical union of citrate and amboceptor, by which the calcium is set free. If it were due to calcium in excess in the guinea pig serum added, the action should be more prompt.

All patients admitted to this hospital by 10:00 A. M. on Mondays and Thursdays are examined by this method and a report made to the Clinic at 2:00 P. M. of these days. Strong positives and decided negatives have a great value in the study of the case. The possible effect of alcohol in producing a negative is eliminated by a subsequent test a few days later. Venepuncture is a severe shock to many nervous cases, though it is still done for the sake of comparison. This test, supplemented with spinal puncture, may prove to give all the information obtainable.

FURTHER NOTES ON A MODIFICATION OF THE NOGUCHI TEST*

By Norman E. Williamson, M.D., Stockton, Calif.

SINCE the complete inhibition of hemolysis should be the only criterion in titration of a syphilitic blood, the presence of demonstrable cells is all that is necessary for this purpose. Since no blood would be titrated which had not already shown complete inhibition in the standard quantity of blood mixture, 1 c.c., the titration may well begin with ¾ c.c. of blood mixture and can be done according to the following table:

A blood I examined gave, when inactivated by the Noguchi system with the standard of 0.08 c.c., complete inhibition with 0.03 c.c. This would be equal to six plus. The same blood titrated by the method here given gave inhibition in the fourth tube which contained 0.0075 c.c. of blood or approximately 0.005 c.c. of serum. This would, according to this method, be 8 plus, so in comparing titration with the fresh blood with former methods, allowance should be made for this difference. It is readily seen in this case that by inactivation the blood had lost ⅝ of its strength in syphilitic reagin. If amboceptors capable of nonspecific fixation lost as much, their action would, of course, not show. Dilution of fresh blood may serve the same purpose of preventing nonspecific fixation.

To save materials and also to get the effect of further dilution, one can use in the standard test, half the quantity of blood, or 0.06 c.c. in 3.94 c.c. salt solution, and use 1 c.c. for each tube. All materials can then be used in

*From the State Hospital, Stockton, Calif.

half strength and the results are excellent. It is well to pay no attention to minor degrees of inhibition of hemolysis.

For survey purposes of old patients in this hospital, I am using only the cholestrinized acetone insoluble fraction as antigen, repeating positives with the non-cholestrinized antigen. This saves material as old cases so far have not shown more than one positive in thirty patients.

Tube No.	Blood Mixture—0.12c.c.blood; 3.88 c.c. salt solution with 4 parts per 10,000 sodium citrate	Antigen-Acetone insoluble fraction, 1 part: Salt Solution 9 parts	Complement	Salt Solution	Shake and incubate ½ hour in water bath at 37° C.	Amboceptor 3 units to 1 c.c.	Shake and incubate 1 hour in water bath at 37° C.	Value of complete inhibition.
1	0.75 c.c.	0.1 c.c.	Units 2	.....		0.8 c.c.		3 plus
2	0.50 c.c.	0.1 c.c.	2	0.25 c.c.		0.6 c.c.		4 "
3	0.375 c.c.	0.1 c.c.	2	0.375 c.c.		0.6 c.c.		6 "
4	0.25 c.c.	0.1 c.c.	2	0.5 c.c.		0.5 c.c.		8 "
5	0.125 c.c.	0.1 c.c.	2	0.625 c.c.		0.5 c.c.		16 "
6	0.75 c.c.	.....	2	0.1 c.c.		0.8 c.c.		Anticomplementary control
7	0.75 c.c.	.....	.....	0.1 c.c. plus amt. of comp.		0.8 c.c.		Measure of human complement
8	0.5 c.c.	.....	.....	0.5 c.c.		.....		Control for cells

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EDITORIALS

The Condition of the Circulatory and Respiratory Systems in Pneumonia

VALUABLE information concerning the state of the heart muscle and of the vasomotor and respiratory centers secured from experiments on animals has been published at various periods during the past two years from the laboratory of Comparative Physiology of the Harvard Medical School. On account of the great importance which the conclusions so far reached must have in the investigation of the disease in man, the following brief review of the work is offered here.

The first paper, published by Porter and Newburgh[1], deals with the state of the vasomotor center in rabbits, cats and dogs exhibiting marked symptoms of pneumonia as a result of infection with the pneumococcus of Fränkel or the streptococcus mucosus (pseudopneumococcus, pneumococcus mucosus). The first mentioned organism was injected intravenously in rabbits, and caused a septicemia, death occurring in from 48 to 96 hours. The pseudopneumococcus was introduced directly into the bronchi through a catheter in all three classes of animals; it caused acute bronchopneumonia, but some of the animals, particu-

larly the cats, ultimately recovered; the others, particularly the dogs, often in about twenty-four hours developed a comatose condition with a marked fall in rectal temperature. The condition of the vasomotor center in animals nearing death was ascertained by measuring the reflex change in blood pressure produced by stimulating depressor or pressor nerve fibers. It was found that the changes were of the same magnitude as those observed by the same methods of investigation in normal animals, thus proving beyond dispute that in animals about to die from pneumonia the vasomotor center is in a normal condition.

The next important paper of the series[2] deals with the condition of the heart muscle in dogs near death or just dead of pneumonia produced by intratracheal injection of B. pneumoniæ (Friedländer). The condition of the heart muscle was determined by observing the work done by a piece of excised ventricular muscle perfused under pressure through the left coronary artery. The piece of muscle was connected with a muscle lever writing on a very slowly moving recording drum, the work done being gauged by the length of the period during which the muscle continued to contract and the total area of the contractions. To secure comparative figures the ingenious device was adopted of cutting out, from cards of uniform thickness, exact patterns of the tracings, which were then weighed. It is not generally known that Porter successfully used the above method for studying the beating of excised mammalian ventricular muscle just twenty years ago, which entitles him to the credit of being the first investigator to succeed in demonstrating that mammalian cardiac muscle maintains its rhythmical contractility outside the body.

Four series of experiments were performed, ten animals being used in each series. The general nature of the experiments and the average results are as follows:

PREPARATION	DURATION OF CONTRACTIONS	TOTAL WEIGHTS OF CONTRACTION AREAS
1. Normal ventricle and normal blood	181 minutes	8.84 gm.
2. Pneumonic ventricle and normal blood	187 minutes	8.46 gm.
3. Normal ventricle and pneumonic blood	70 minutes	3.40 gm.
4. Pneumonic ventricle and pneumonic blood	176 minutes	6.46 gm.

The results clearly demonstrate that in pneumonia the heart muscle is perfectly normal when it is fed either with normal blood (2) or with pneumonic blood (4), but that the efficiency of a normal heart is strikingly lowered when it is supplied with pneumonic blood (3). Two conclusions of the greatest consequence are thus permissible: the first, that the heart muscle is not functionally impaired in pneumonia; and the second, that this nonimpairment is due to the muscle having acquired some sort of immunity towards the poisonous influence which, as the results of the third series of experiments show, pneumonic blood exerts on normal cardiac muscle.

Having shown that neither the vasomotor center nor the heart muscle is affected in pneumonia, direction was centered on the behavior of the respiratory center.[3] The reason for choosing this as the next step to take in the investigation was the fact, often observed by the authors during the work described above, that the respirations frequently failed while the heart and vasomotor center were normal. The condition of the respiratory mechanism was, therefore, com-

pared in healthy dogs and cats with its condition in animals infected with pneumonia (B. pneumoniæ of Friedländer, and, in one case, the pneumococcus).

The activity of the respiratory center was studied by observing the volume of air passing into and out of the lungs while the animal breathed through a tracheal cannula, and (Tissot) valves, into a graduated (Gad) spirometer and out of a bottle, the bottle and spirometer being also connected by tubing so as to form a closed system. The spirometer was caused to record its excursions on a drum. As the CO_2 increased in the air of the system—determined by removing samples for analysis—the curve became deeper until the maximum reaction was reached. It was found that anesthetics materially depressed the reactivity of the center in normal animals, but that decerebration had no effect (after allowing the influence of the anesthesia necessary for the decerebration to pass off). The observations were, therefore, made on decerebrated animals except in the case of dogs in which the pneumonia had gone so far as to make them comatose. The average percentile increase in tidal air in normal decerebrated dogs as compared with pneumonic dogs *with the same initial ventilation* was found to be as follows:

CO_2 PER CENT IN AIR OF SYSTEM	PERCENTILE INCREASE IN C.C. AIR BREATHED.	
	Normal	Pneumonic
1	17	15
2	43	35
3	90	57
4	148	74
5	216	85

It was shown that the mechanical effect of the consolidation of the lungs was not responsible for these results; thus, they were not obtained after injecting starch into the bronchi, nor was the fall in excitability of the center in the pneumonia cases proportional to the degree of consolidation of the lungs. The degree of depression of the center was found to be proportional to the stage of the disease. By making a division into mild and severe cases, as determined by the behavior (lowering) of the rectal temperature, such results as the following were obtained:

REACTION TO 5 PER CENT CO_2	PER CENT
In normal dogs (with varying initial ventilation)	
In moderately ill dogs	127
In gravely ill dogs	68

Perhaps the most interesting of the papers is the last to be reported[4], in which the possible causes for the depression of the respiratory center are investigated. Using the above described method for testing the excitability of the center, it was found that intravenous injection of the cultures of the B. pneumoniæ into a normal dog did not cause depression, neither did injection of blood from another animal dying of the disease. These two observations show that the poisons produced in the blood by the growth of the organism are not the cause of the depression. The possibility next considered was that inadequate oxygen supply to the center might lower its excitability, the cyanosis so commonly observed as one of the symptoms of pneumonia giving some

weight to the suggestion. Experiments of various types were performed to test it; thus, pneumonic animals were supplied with an excess of oxygen by keeping them for long periods of time in a box ventilated with air containing several times the normal percentage of oxygen, but with entirely negative results, for neither was the progress of the disease checked, nor the condition of the animal materially improved, nor any change noticeable in the frequency or the depth of the respirations. Attempts to administer the oxygen by slowly injecting it into a capillary area (through the femoral artery) were disastrous, for the oxygen formed air emboli, which could be seen through the exposed femoral vein and which quickly killed the animal. These experiences do not offer much support to the clinical practice of oxygen administration in pneumonia. That oxygen starvation of the center could not be held accountable for the dyspnea was further shown by the inability to demonstrate a similar degree of dyspnea after reduction of the number of red blood corpuscles by hemorrhage or by combining some of the hemoglobin with carbon monoxide (by mixing illuminating gas with the inspired air).

It was also attempted to conserve the animal's strength and so prolong life or permit "the crisis" to be tided over by applying forced respiration by means of an artificial respiration apparatus, but again with entirely negative results; indeed it was found that the animals went on breathing at the usual (pneumonic) rate and depth in spite of the forced respirations. To make it perfectly certain that the depression of the center could not be due merely to its exhaustion as a result of the frequency and excessive intensity of its discharges, a condition of dyspnea was induced in normal animals by causing them to respire for several hours in an atmosphere containing an excess of carbon dioxide (with abundance of oxygen), and then removing them and, when the breathing had returned to normal, testing the response of their respiratory center by the above described method. It was found to be normal. Mere fatigue of the center cannot, therefore, be the cause of its depression in pneumonia.

In the face of so many negative results, it seemed as if no definite cause could be discovered to account for the dulling of the respiratory center, but a clue was secured by piecing together certain of the above observations; thus, that no dyspnea occurs when there is no inflammation of the lungs, although fatal bacteremia is present, as after intravenous injection of B. pneumonia, and that such does occur when inflammation of the lungs is present, as when the bacillus is administered intratracheally, indicates clearly that it is not because of any toxic substance in the blood that the center becomes dulled, but rather that the inflammatory condition of the lungs of the same animal is the responsible factor. The question remains as to how the condition in the lungs comes to act on the respiratory center. Two pathways are open between the lungs and the center, the blood and the vagus nerves. The former is ruled out as concerned in connection with pneumonia, because blood from a pneumonic animal does not cause dyspnea when injected into one that is normal. By exclusion, then, it would appear that the association is affected through the vagus nerves, and it is certainly to be considered as one of the most interesting results

of recent research in experimental medicine that the authors should have succeeded in showing, by direct experiment, that this conclusion is the correct one. In short, they found that the excitability of the respiratory center to carbon dioxide—as measured by the above described method—is the same in vagotomized pneumonic dogs as in normal animals. In the vagotomized animals it was also observed that there is no dyspnea, and that the fall in the rectal temperature, usually observed shortly before death, was often absent, sudden death being, however, not infrequent.

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—*J. J. R. M.*

Commercial Glucose As a Food

WESENER and Teller[1] have recently reported a study of the chemical and digestive properties of commercial glucose. This term is applied to a product obtained by the action of certain catalytic agents upon refined starch, continued until the starch is converted into a mixture consisting principally of glucose, maltose and dextrins. The digested mass is purified by bone-black and then evaporated to a syrup. In this country cornstarch is used exclusively and the product is known as corn syrup. Wesener and Teller describe this preparation as follows: "Commercial glucose is a complex body of viscous consistency, running about 42 to 45° Beaumé, and containing 80 to 85 per cent of solids and 15 to 20 per cent of water. It is nearly water-white and possesses a mild sweet taste. The solids are composed almost wholly of sugars and dextrins, a minor portion consisting of a trace of mineral matter. The ash, present to the extent of mere traces, consists of mineral salts, including phosphates, sulphates, chlorides and carbonates, chiefly of sodium and lime. Tests for arsenic and other poisonous metals show these not to be present. Nitrogenous substances are present as mere traces, chiefly as protein bodies, amounting to about 0.06 per cent."

The sugars fermentable with baker's yeast are a mixture of maltose and dextrose, these varying in different preparations from 11.7 to 17.2 per cent of dextrose and from 22.9 to 16.4 per cent of maltose. There is a third substance which is less readily fermentable by ordinary baker's yeast but which is made fermentable by the action of certain enzymes, notably those present in pancreatin, Taka-diastase and malt, also by dilute hydrochloric acid under the influence of heat. This substance amounts to about 14 per cent of the glucose, when calculated as maltose, and about 8 per cent when calculated as dextrose. The unfermentable bodies after the removal of the substances above mentioned

consist of those bodies generally denominated as dextrins, and these after subjection to the hydrochloric action of diastase are converted into substances which under suitable conditions undergo almost complete alcoholic fermentation. Likewise, these dextrins after being acted upon by hot dilute acid become wholly fermentable. A good quality of Taka-diastase converts the unfermentable bodies into fermentable sugars, leaving only a small amount of unfermentable residue, which contains less than one per cent of the glucose taken. Pancreatin of good quality has a like effect, but in some instances the conversion was less complete than with Taka-diastase.

A comparative study was made of the action of hydrolytic agents, including enzymes, on commercial glucose and our chief carbohydrate foods, such as potatoes, breakfast cereals, bread, etc., and upon pure starches obtained from these foods. In these comparisons it was found that the carbohydrates of glucose agree closely in gas production with the carbohydrates of ordinary foods. When the latter are acted upon by isolated ferments and yeast they yield variable but appreciable amounts of unfermentable products.

Wesener and Teller conclude their report with the following statement: "The fact that commercial glucose, when it is treated with diastase and then subjected to yeast fermentation, is almost wholly converted into alcohol and carbon dioxide, goes to prove that it consists of products that are wholly assimilable, and, therefore, it furnishes a food to the body of a sugar nature. In this respect it is a more concentrated and at the same time a more readily assimilable food than are most of the carbohydrates belonging to the ordinary foodstuffs which first have to undergo cooking and then complete hydrolysis by the action of the digestive enzymes before they can be utilized by the body. In this respect glucose, pound for pound of dry weight, will furnish at least as much energy as does cane sugar."

Carlson, Hektoen, and LeCount[2] have studied the effects of commercial glucose when fed to white rats. Four groups of twenty-five each were fed on glucose bread; two groups of the same number each on cane sugar bread, and two groups on sugar-free bread. The feeding was continued through six months, a period of about one-sixth the average length of life in this animal. The quantity of glucose consumed each day by those fed on the glucose bread amounted to from 2.5 to 3.5 g. per kilo body-weight. "A parallel test on a group of persons weighing each 60 kilos and living sixty years on the average would mean a daily consumption of 150 to 200 g. commercial glucose per day for ten years." The animals were kept twenty-five in a cage and the ration to begin with for each cage consisted of 300 g. of bread, 150 g. of carrots, or of meat occasionally, and plenty of water. All debris was removed and a new supply of food given at a certain hour each day. As a rule the day's supply was wholly exhausted with the exception of the hardest bread crusts. After about one month the daily ration was increased, the same in each cage. The animals did not wholly escape infection and some succumbed to pneumonia and so-called rat-typhoid, but one group did not suffer from infection more than the others. Weighings were made every two weeks and the results showed that weight increased at practically the same rate in each group. In the course of

the experiment two rats of each group were injected intra-abdominally with 5 c.c. of a ten per cent suspension of sheep corpuscles per kilo of rat weight and six days later these animals were killed and the production of antibody determined. All groups corresponded in this particular and showed no difference from rats kept under usual laboratory conditions. The fecundity of the glucose-fed rats was slightly greater than that of the other groups.

These investigators state their conclusions as follows: "The addition of commercial glucose in the amounts of about 2.5 to 3.5 g. per kilo body-weight per day to the diet of white rats for a period of six months has no abnormal influence on the animals, either favorable or unfavorable, as determined by the rate of growth, fecundity, immunity reactions and the condition of the organs. As both the glucose-fed and the control groups were kept on a liberal diet throughout the observation period, the experiment does not show to what extent the commercial glucose was actually absorbed and oxidized, but in the quantities fed, the commercial glucose certainly has no injurious effects."

Sansum and Woodyatt[3] have used phlorhizinized dogs to determine to what extent the carbohydrates of commercial glucose are absorbable and convertible into d-glucose and consequently to what extent they are utilizable in the organism. "The idea suggested itself of passing a food through the body of a completely phlorhizinized dog and measuring its total yield of extra sugar in the urine, the well known phlorhizin technic being thus applied to a problem of food analysis. The extra sugar recovered would then naturally represent nothing which was either indigestible, unabsorbable or unassimilable."

With this idea these investigators fed completely phlorhizinized dogs with pure d-glucose and with commercial glucose and determined the extra sugar which appeared in the urine in each case. Theoretically all the d-glucose may be recovered in the urine, but practically in their experiments, only 74.6 per cent was so recovered, while 71.29 per cent of the commercial glucose was recovered. "On the basis that the sample of commercial glucose submitted for study contains 20 per cent of water, 100 g. of the solid residue is capable of affecting the urinary out-put of d-glucose from completely phlorhizinized and glycogen-free dogs in the same manner as though it contained 95.48 per cent of pure d-glucose. This implies that at least 95.48 per cent of the solid matter in the sample of commercial glucose studied is capable of passing through whatever physiological processes of digestion, absorption, and assimilation are necessary for its ultimate existence in the body as d-glucose."

"The animals showed no evidences of any deleterious effects attributable to the ingestion of commercial glucose, notwithstanding the large size of the doses (1 to 2 g. per kilo of body weight in three to six hours) and the great sensitiveness of completely diabetic animals to toxic influences."

One can only conclude from the evidence brought forward by the several investigators above quoted that Mendel[4] is justified in the following statement: "Corn syrups and glucose sugars artificially prepared from cheap sources of starch have survived the propaganda of prejudice and now represent one of the cheapest sources of wholesome nutriment."

There is nothing deleterious in commercial glucose as now prepared. It

consists of carbohydrates, which are in part predigested and in part partly digested. All of these are, after the completion of alimentary digestion, absorbable and assimilable and capable of supplying the body with energy. In short they comply with all the requirements of a healthy food. The average man needs in his daily ration about 540 g. of carbohydrates. It is best, indeed it is quite essential, that his daily ration should consist of mixed carbohydrates. If he took it all in the form of plain starch, his digestion would be overtaxed. If he took it all completely digested it would be absorbed so rapidly that the blood would be flooded with it and glycosuria would result. If he took it all in the form of cane sugar it would be too sweet and besides intestinal irritation would result. By thorough cooking of starchy foods man secures their partial digestion and their more ready absorption. Commercial glucose consists of partially digested carbohydrates and if a higher degree of sweetness is desired it may be mixed with cane sugar.

While the former is a manufactured product, the hydrolytic changes brought about in its preparation are identical with those occurring in the alimentary canal; consequently its predigested and partly digested constituents correspond to stages reached in the normal digestion of carbohydrates and supply the body with similar sources of energy. Commercial glucose may be regarded as a wholesome and nutritive food and may be mixed, as taste or fancy may dictate, with other carbohydrates in the preparation of the daily ration.

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—*V. C. V.*

Some New Facts Concerning the Adrenal Glands

THERE is no subject in physiology that has attracted more attention in recent years than has the function of the adrenal glands. This interest has not been confined alone to the medical profession, for we find several semi-popular books in which attention is given to the relation which these glands bear to many of the functions of the human mechanism. The effects of the removal of the glands from the body are so drastic, and the physiological action of the substance, epinephrin, which they secrete, is so widespread and apparent that the importance of the glands cannot be questioned. Any new facts which add to our knowledge, or any experiments which disprove existing theories concerning the working of the glands are surely most welcome, for there is still much uncertainty as to the normal function of epinephrin and the conditions under which it is secreted into the blood.

Recent work has impressed one with the idea that the adrenal glands besides continually secreting some adrenalin into the blood, act, as it were, as

emergency auxiliary organs to the sympathetic nervous system, and in time of stress, pour out an increased amount of epinephrin into the blood. As examples and proof of the ultility of such a mechanism, the effect that epinephrin has on increasing the amount of blood sugar is cited, and the occurrence of emotional hyperglycemia is attributed to the extra epinephrin which is poured out into the blood during great nervous excitement. Again, stimulation of the splanchnic nerves, emotional excitement, and injections of epinephrin all decrease the clotting time of blood, an obvious advantage to animals in combat. Morphine is known to reduce the amount of epinephrin which can be collected from the glands of a cat. This action is supposed to be due to the fact that morphine excites the cat and that this excitation brings about a depletion of the epinephrin in the gland by stimulation of the secretory nerves of the gland.

A recent paper by Stewart and Rogoff* upon the influence of certain factors, especially emotional disturbances upon the epinephrin content of the adrenals, throws some new light upon the relationship of these glands to the central nervous system. These investigators could obtain no evidence that there is a decrease in the amount of epinephrin which can be obtained from the adrenal of the cat after prolonged emotional disturbance produced by frightening with a dog; nor could they obtain any evidence that the depletion of epinephrin in the adrenals following the administration of morphine is due to the attending nervous excitement. All the signs of morphine fright was observed in cats in which one adrenal was removed and the nerve supply of the other gland destroyed, thus establishing a condition which is known to protect the adrenal from morphine depletion. Moreover, dogs respond to morphine without excitement, and yet when given the alkaloid, marked depletion occurs in the epinephrin content of their adrenal glands. Evidently, therefore, excitement is not the cause of epinephrin depletion following morphine administration.

β-tetrahydronaphthylamine administered to cats has been shown by Elliott to cause a marked depletion of the epinephrin store in one gland, the nerve supply of which is intact as compared to its fellow, the nerve supply to which has been previously cut. This effect he believed to be due to the emotional excitement which seems to accompany the injection of this drug in the cat. Stewart and Rogoff were able to confirm Elliott's experimental observation, but failed to obtain similar results with the rabbit, which apparently reacts to the drug as does the cat. In the case of the rabbit, both glands; i.e., the denervated and the normal gland, suffered some depletion of their epinephrin store. Evidently the action of β-tetrahydronaphthylamine on the adrenals in the rabbit differs from its action in the cat.

Another very important observation which these authors make concerns the reactions which occur in the denervated iris of the cat under conditions which have been thought to produce a hyperepinephrinemia. The denervated iris responds with dilation to very small doses of epinephrin, and this reaction has been used as a delicate test for epinephrin in the blood. Stewart and Rogoff were not able to demonstrate any difference in the character of the reactions

*The Jour. of Exp. Med., 1916, xxiv, p. 709.

of the denervated iris elicited under conditions supposed to produce an outpouring of epinephrin in cats either normal or in which one adrenal had been removed and the nerve supply of the other gland destroyed some days previous to the experiment. By doing the experiment this way the otherwise fatal issue of double adrenalectomy is avoided.

Marked depletion of the epinephrin store of the innervated glands as compared with the denervated gland was observed in animals dead or dying from infections of various kinds. Stimulation of the splanchnics, a condition known to produce a hyperepinephrinemia, does not deplete the store of epinephrin in the gland except after very prolonged stimulation. Evidently splanchnic stimulation not only affects the discharge of adrenalin into the blood but also increases the rate of epinephrin formation.

We must conclude from this work that there is a difference in the type of response of the adrenals to conditions which deplete the store of epinephrin in the gland, and to those conditions which are supposed to be accompanied by an increased out-pouring of epinephrin into the blood. There is evidently one mechanism which controls the formation of epinephrin in the adrenals and another mechanism which conditions its secretion into the blood.

—*R. G. P.*

Epilepsy.

A RECENT series of communications in current medical journals is concerned with the bacteriology of epilepsy, a subject first brought to attention by Bra in 1902, revived by Reed in 1914, and enlarged upon by the latter author in 1915 and 1916.

Reed has built his conceptions of the etiology of epilepsy upon the fact that constipation and epilepsy are associated in a large number of cases; and upon the theory that the constipation is the result of greater or less atony of the intestinal walls, especially those of the large intestine, or upon interference with the movements of the intestine because of abnormalities of positon, or both. Evidently his whole point of view has been largely influenced by the opinions of Arbuthnot Lane. Once stasis has been produced, Reed believes that the body (the blood stream) is invaded by bacteria from the intestinal tract and these bacteria produce, by means of toxins, or by their presence in the central nervous system, the series of symptoms which we call idiopathic epilepsy. In proof of this theory of infection, he[1] and his assistant, Dr. Hyatt, report the very consistent finding of a peculiar organism in blood cultures which they say is identical with that originally cultivated by Bra, and which, from descriptions, is not clearly different from Bacillus subtilis. With pure cultures of this organism they are able to produce convulsive conditions in rabbits by introducing it into the ear veins.

Since Reed's reports, Wherry and Oliver,[2] Caro and Thom,[3] and Terhune,[4] have reported investigations aimed to discover more of the facts regarding the events associated with epilepsy.

The report of Wherry and Oliver is, as they acknowledge, a limited one. Nevertheless, working with Dr. Hyatt, they were unable, using the most modern methods, to discover any evidence of blood infection in four of Reed's cases. In a fifth case, one culture tube, in a series of ten, showed a growth which Reed reported contained B. epilepticus.

Caro and Thom reported their work with seventy cases from which 160 cultures were made with completely negative results except in four instances in which contaminations appeared. The contaminating organisms did not correspond with B. epilepticus. Moreover, Caro and Thom report that in 17 necropsies on epileptics, Canavan was unable to find any organism resembling B. epilepticus.

Terhune, on the other hand, reported that in his series of blood cultures from 24 cases of epilepsy he was able to isolate a bacillus, identical with Reed's, in 75 per cent of his cases. With this organism he was not able to cause convulsions in rabbits but was able to do so in cats.

Reed,[5] in a recent polemic, comments upon the work of those who have not been able to confirm his results, especially in the case of Wherry and Oliver, and says that "the assumption or inference that the organism does not exist is hardly tenable." No writer with whose work the reviewer is acquainted has said that the organism does not exist—they say they could not find it, when they didn't find it. Reed mentions confirmations of his work by various men at various points, but in no case are the details of their work known. As a matter of fact, the work that has been published on this subject from well organized laboratories in charge of well known workers concerning whose methods there can be no suspicion, is consistently negative.

This does not mean that the facts of Reed, Hyatt and Terhune are not true, but the fact that discrepancies are present makes it obvious that more systematic work should be done, preferably in large institutions supplied with every facility, and by thoroughly trained workers.

It is to be hoped that if the finally accumulated evidence is positive, the laboratory workers will not complain that the facts have been "beclouded by a policy of concerted and cumulative" affirmation.

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[4]Terhune: Ibid., p. 1155.
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—*P. G. W.*

The Factors Which Determine the Adequacy of a Vegetable Diet

THE factors which determine the adequacy of a vegetable diet are of great interest especially now when we are hearing much of meatless, eggless, milkless, and butterless days. Moreover they are of vital concern to the medical man in the consideration of the so-called deficiency diseases. The vegetarian who religiously refuses all meat, eggs, milk, butter, etc., imposes upon

himself the necessity of wisely choosing from the staple vegetables a diet adequate to support growth and to maintain health. There can be no doubt that vegetable foods contain the factors essential for complete nutrition. The grazing animals grow entirely from food of plant origin. Nevertheless the vegetable foods ordinarily consumed by human beings lack several dietary factors, or contain them in inadequate amounts. It is, therefore, necessary to have some technical knowledge of food values if one wishes to choose a balanced vegetable diet. There is an accumulation of evidence to show that the seeds of any one of the common food plants do not maintain growth or support well-being when fed even in large variety. On the other hand by choosing proper proportions of a limited number of these seeds practically complete development may be obtained in the experimental animal. This observation shows that instinct, when the diet is confined only to the seeds of the common vegetable foods, is not a safe guide to complete nutrition.

McCollum and Davis[1] working with purified food substances found that besides protein, carbohydrates, fats and inorganic salts, two other substances were necessary. For these compounds they propose the terms, "Fat soluble A.," and "Water Soluble B." The former they find in great abundance in butter fat, and yolk of egg, and in fair amounts in meats and the leaves of forage plants. It is also present, although in inadequate amount, in many cereal seeds, corn apparently possessing a fair amount. The Water Soluble B. is present in many plants and is especially plentiful in the wheat embryo. McCollum and Davis believe that these factors are the same compounds which Funk has termed "Vitamins" and which this author believes include several dietary constituents of unknown chemical composition. They believe, however, that it is unnecessary to assume as Funk does the existence of more than the two factors above mentioned and are convinced that all the pathological phenomena can be accounted for by maladjustments relating to the following factors:—poor quality and inadequate quantity of the protein content; shortage of the substances A or B, or both of them; or the presence of some toxic substances in the natural food stuffs of inorganic or organic nature; or lack of inorganic salt.

McCollum, Simmons, and Pitz[2] in a recent article present data which they believe will at least serve to orient investigations on the question of nutrition by natural foodstuffs. They have tested fully three natural foodstuffs; viz., wheat, wheat embryo, and rice, upon a working hypothesis which postulates the need of but two chemically unidentified factors; i. e., A. and B. above described, in addition to the well-recognized constituents, proteins, carbohydrates, and inorganic salts. The results in the case of wheat are briefly shown in the following table; they offer an interpretation of the ways in which a food stuff may give rise to metabolic disturbance. The experiments were conducted upon different groups of young rats. Butter fat was fed to furnish the Fat Soluble A. substance. The embryo of the wheat contains sufficient Water Soluble B. substance. The protein was pure casein.

[1]Jour. Biol. Chem., 1916, xxiii, 231.
[2]Am. Jour. Physiol., 1916, xli, 333.

	RATION.	RESULTS.
1.	Wheat kernel	Fails to support growth
2.	" " + salts	" " " "
3.	" " + " " + protein	" " " " to maturity
4.	" " + butter fat	" " " "
5.	" " + " " + salts	Animals inactive, growth deficient
6.	" " + " " + protein	Fails to support growth
7.	" " + protein	" " " "
8.	" " + " + butter fat + salts	Supports growth and maintains well being.

The above results give a complete picture of the dietary deficiencies of the *wheat* kernel. Its proteins are of poor quality, it lacks the Fat Soluble A. substance, and has a deficient salt content.

Wheat *germ* was found to contain proteins of good quality, but to be deficient in salts and the Fat Soluble A. substance. Besides it was found to contain an oil which has a depressing effect upon the health and growth. The dietary deficiencies of polished rice were studied systematically as in the case of the wheat kernel. Rice was found to be lacking in proteins, inorganic salts, and in both the unknown chemical substances, A. and B. The existing data together with some experiments on the dietary factors present in corn, led these writers to conclude that the corn kernel contains proteins of poor quality, less than the required amount of the Fat Soluble A. substance, and an inadequate salt content. It contains a liberal supply of the Water Soluble B. substance.

From these experiments it is evident that the lack of a single factor will bring an animal into a pathological condition; or a toxic substance, such as that found in wheat embryo, will cause nutritive failure. The authors point out the fallacy of the assumption that the safest plan to assure perfect nutrition is to include a wide variety of foods in the selection of the constituents of the diet. Variety may make for safety, but the optimum result will not be obtained in a considerable number of cases. A knowledge of the specific properties of our natural food stuffs and their supplementary relations to each other will perhaps enable one eventually to compound simple and adequate diets of purely vegetable origin.

—*R. G. P.*

Carriers and Gall-Bladder Infections

IN the group of diseases comprised of typhoid, cholera, and bacillary dysentery, one of the most important problems of preventive medicine seems to be the prevention and cure of gall-bladder and gall-passage infections. The prominence and importance of such infections in typhoid has been known for a long time; in the other instances it is less appreciated. Nevertheless several writers who have studied cases of semichronic intestinal carriers have shown that the carrier aspect was due to infection of the gall-bladder. In a few cases of bacillary dysentery the infecting organism has been recovered from the bile.

This subject of gall-bladder infection has been approached by Nichols* from the experimental point of view. The experimental animal was the rabbit which was used because "in some respects, at least, the lesion in the rabbit is a counterpart of that in man, and it seems probable that, in working out means of preventing and curing carriers, the experimental lesion in the rabbit will be an important factor." Nichols' report deals with the mechanism of gall-bladder infections.

Nichols calls attention to the fact that in typhoid a gall-bladder lesion might be due to descending infection of the bile from the liver, to an ascending infection from the intestine, or to a transverse infection through the gall-bladder wall by way of the blood vessels. Previous to the time of Koch, the descending pathway was the generally accepted one, but since 1908 the transverse pathway has been that of choice. That ascending infection is not a common affair may be realized from the infrequency of colon infections of the gall-bladder. The same questions regarding the route of the infection arise in connection with cholera and dysentery.

As a result of his carefully planned experiments, Nichols arrives at the following conclusions: The theory of the production of gall-bladder lesions in typhoid by descending infection of the bile from the liver, receives support. More bacilli appear in the bile with increased doses and more gall-bladder infections are obtained by increased doses. More bacilli appear in the bile after mesenteric vein injection than after ear vein injection and more lesions result under the first condition. More bacilli appear in the bile after injection of the same dose in immunized animals than in normal animals and more lesions also result in immunized animals.

In cholera and dystentery the same mechanism is suggested with the additional factor of a portal system septicemia.

After the appearance of microorganisms in rabbit bile, their fate is apparently largely determined by the antiseptic properties of the bile. The antiseptic action is largely due to alkalinity. It is apparently possible to protect the rabbit to some degree against gall-bladder infections by a previous injection of sodium bicarbonate, and therefore alkali therapy is suggested in the prevention and cure of gall-bladder carriers.

—*P. G. W.*

Ritual Murder

THERE is a superstition prevalent among the more ignorant Christians of Southeastern Europe and Asia Minor that the Jews offer human sacrifices, and that they prefer young Christians, especially girls, for their victims. This superstition has a strong hold in certain localities, and is today a fixed belief held by many Syrian Christians, especially those living in Damascus. They bring this belief with them to this country, but, so far as we know, it has not led to any medico-legal investigation here. However, in Hungary and Bohemia it has led to criminal charges. One of the most celebrated cases of this

*Nichols: Jour. Exper. Med., 1916, xxiv, 497.

kind is that known as the criminal process of Tisza-Eslar, which is a small community in Northeastern Hungary. On April 1, 1882, a servant girl, aged 14 years, 3 months and 23 days, was sent to the village to buy some colored yarns. It was found on inquiry that she made the purchase but did not return home. Indeed, she disappeared and the closest search failed to reveal any trace of her. On the day of her disappearance the Jews of the neighborhood held a religious ceremony at their temple in the village. The ignorant Christians began to suspect that the Jews had used the girl in their sacrificial rites, and about the end of April a little boy, aged 4 years and 9 months, a son of an attendant at the temple, reported that he had seen his people, the Jews, sacrifice the girl. At one time he said that she was bled from the thigh and another time that her throat was cut. The temple attendant and three other Jews were arrested and charged with the crime. Another son of the attendant, 13 years old, was questioned and at first denied any knowledge of the girl, but later he told that he had helped murder her. On the 18th of the following June a female body was found in the river below the village. She had on the clothes of the lost maid, and even carried on her arm a little bag containing the colored yarns which the girl had purchased the day of her disappearance, but the relatives and friends of the girl said that the body found in the river was not that of the lost girl. The head of the corpse found in the water was bald, and it was claimed that it had been shaven. The lost girl had done hard manual labor, and her hands were coarse, the skin thickened and callous, and the nails unkempt. The water corpse had beautiful white hands with tapering fingers and delicate nails. The local experts pronounced the corpse as that of a woman not less than 18, and most probably 20. It was claimed that the Jews had murdered the girl and had now gotten another body, probably by a second murder, had clothed this with the garments of the lost girl, and had thrown it into the river to lead the people to believe that the girl had been drowned. The local experts claimed that the body found had been in the water but a few days. At last some intelligent men were brought from the University of Koloszvar and others were called from Vienna and Budapest, and it was shown that the body was that of the lost girl, that it had been in the water so long that it had been partly changed into adipocere, and that the beautiful hands and tapering fingers were due to the fact that the epidermis had been removed by maceration, and that the scalp had been deprived of its adornment by the same process. It should be stated that the final examination was made in December, 1882, the body having been buried in dry sand from the previous June, when it was found in the water.

—*V. C. V.*

Vitamins, Diet, and Beriberi

BY the term "Vitamin" we have come to mean a chemical substance which is a constituent of certain foods, which in almost infinitesimal amounts has a beneficial influence upon the course of certain diseases, and which is an essential constituent of a normal diet. When such a substance, or substances, are eliminated from a diet, disease occurs. When it is added to an otherwise

vitamin-free diet the disease does not appear. When it is used therapeutically, the disease improves and health returns. The vitamins have been studied exhaustively especially by Funk and others, particularly in connection with the disease beriberi. It is with reference to this disease and its relations to vitamins that Vedder has contributed a recent interesting discussion.*

From the time when Eijkman discovered that fowls develop a condition very closely resembling beriberi (polyneuritis gallinarum) if they are fed upon an exclusive diet of polished rice, interest in the so-called deficiency diseases has increased, and much energy has been expended upon experimental work designed to determine the means by which the pathologic effects are produced It became plain, that many, at least, of the cases of beriberi studied were associated with the use of polished rice; i.e., grain which had been milled to the point where the whole pericarp had been lost, and only the polished carbohydrate kernel remained. It was later shown that persons might be fed upon polished rice with no evil effects provided a quantity of the husks removed by polishing were added to the ration, and also that unpolished rice did not conduce to disease. Still later, Fraser and Stanton showed that a protective substance might be prepared in solution from rice polishings by treating them with 0.3 per cent hydrochloric acid solution, and later Chamberlain and Vedder showed that the active substance was soluble in water and alcohol, but that it was insoluble in ether, that it was dialyzable, and that extracts of polishings containing only the water and alcohol soluble substances would cure infantile beriberi with marvelous rapidity. Then Funk obtained from rice polishings a crystaline base which would promptly cure fowls suffering from polyneuritis. It was for this substance that Funk coined the name *Vitamin*. Other workers studying this and allied substances of other origins, obtained materials which were different in composition from Funk's, but which were similar in pharmacologic action—hence the term, *Vitamins*. It then appeared that a pure crystalline *vitamin* had not been produced. Williams next attacked the subject from the synthetic standpoint and prepared substances which had decided antineuritic qualities.

It is obvious from the whole mass of evidence up to the present time, that these vitamins, whatever they may prove to be, are important factors in diets, which are essential in preserving the health of the individuals. Their absence is responsible for such deficiency diseases as beriberi, scurvy, and possibly pellagra.

Vedder says that the deficiency in the dietary that causes beriberi is not by any means limited to rice, for it has been shown repeatedly that too exclusive diets of ordinary white flour, canned goods which have been sterilized, and most carbohydrate foods, will produce polyneuritis in fowls, and beriberi in man. Rice, so far as is known, has not been shown to produce scurvy in man or animals, but with this exception practically all the "beriberi foods" have been associated with scurvy. Also it is noteworthy that where pellagra is prevalent in the United States, the sufferers from that disease are living very largely on articles that have been demonstrated to produce beriberi or scurvy, or both.

—*P. G. W.*

*Vedder: Jour. Am. Med. Assn., 1916, lxvi, 1494.

Medico-Legal Investigation of the Causes of Death

THE writer has had an experience of many years as an expert in murder cases. This experience leads to the following statements, which may be of interest to physicians called upon to investigate the cause of death in suspected homicide.

Our criminal law fails to give directions concerning many points, and custom has apparently established no definite and satisfactory rules covering these matters. In my experience it has frequently happened that the initiative has been taken by friends or relatives of the deceased, sometimes by those financially interested, such as claimants to inheritance and insurance companies with which the deceased carried insurance; and in at least one celebrated case the initiative was due to the efforts of the man who finally was tried and convicted of the murder. It has not infrequently happened that officials permit some interested party to have full charge of the investigation of the cause of death, or to "work up the case." In most instances this has been due to the fact that the official, thinking that the suspicions were not well supported, has been unwilling to burden the county with the necessary expense, and has been ready to turn over the matter to anyone who would assume the financial responsibility of carrying out the investigation. In this way, it has happened that the obduction of the body and the toxicological examination have been wholly under the control of interested parties. While custom apparently permits this, it cannot be denied that such a procedure may subsequently give rise to much embarrassment in the prosecution of the case, and it certainly would be better for the proper officials to keep the investigations as to the causes of death under their own direction and to forbid participation in these investigations by all interested parties.

A few illustrations along the lines mentioned above may not be devoid of interest. In one instance, the behavior of the man whose wife had recently died gave occasion for much talk in the community, and the husband went to the prosecutor and asked that he be permitted to exhume his wife's body and have certain organs submitted to a toxicologist in order that he might be in a position to vindicate himself. This permission was granted. The husband, a physician, practically had charge of the investigation, and after the body had been exhumed and the stomach removed, he and an undersheriff took this organ to a toxicologist. The husband expressed some doubt as to which of two chemists he preferred and the stomach was left with one chemist with the request that nothing was to be done with it until further orders. A week later this chemist received a written order from the husband to deliver the stomach to the undersheriff who came alone this time. On the same day a stomach was placed in the hands of the second chemist, who examined it and reported it free from poison. However, it soon developed that the husband had obtained a stomach from the city physician of the place in which the second chemist resided. At this point the prosecutor saw that he must take the matter in hand himself. With a physician he went to the cemetery where the woman's body had been buried. Upon opening the grave the coffin was found to be empty. The body had disappeared. Search over the neighborhood failed to reveal any trace of it. With matters in this condition the husband was tried for the murder of his wife. A

shrewd lawyer, who defended him, declined to make any defense. He claimed that the prosecution had failed utterly. The only analysis which had been made had shown the entire absence of any poison. There was, therefore, the lawyer claimed, no evidence against his client. The judge permitted the jury to decide the case and the result was a split jury. Nearly a year later the body of the dead woman was found crowded into a barrel and hidden under a strawstack. The prosecutor was notified, but was never able to show who disposed of the body in this manner. The liver and other organs of the dead woman were examined by a third chemist and found to contain traces of arsenic. A second trial resulted in the conviction of the husband. Owing to certain technical errors, the Supreme Court ordered a new trial. This trial resulted in a split jury, and the husband who had stood three trials soon became insane and died in an asylum. It is not within my province to express an opinion concerning the guilt or innocence of the accused husband. One thing is quite certain, he was insane before he was tried at all. Whether he was insane or not at the time of his wife's death I cannot say. Through the bungling of the officials the county was saddled with the expense of three trials and the final result was no decision as to the man's guilt or innocence.

In the second case the prosecutor and a young physician, neither of whom knew anything about the proper procedure in such a case, resurrected the body from a country burial ground, took it to a shed nearby the village, and there, surrounded by men, women and children from the village, made the obduction. These officials had failed to provide themselves with receptacles for the tissues to be taken and examined, and the prosecutor asked one of the inhabitants of the village who kept a grocery store to bring from his store some fruit jars. The tissues selected for examination were put in these jars without having been even cleansed or even thoroughly inspected by the prosecutor or the physician making the obduction. Arsenic was found in large amount. When the case came to trial it was easy enough to show that the grocer who furnished the jars had not at all times been on friendly relations with the accused, and the suspicion that the grocer might have placed arsenic in the jars was brought into the case.

In the third case the body of the woman was found in the water. Her life was insured and the insurance company offered to relieve the county of any trouble or expense that might be involved in the investigation. The whole matter was turned over to the insurance company. Its agents made the obduction and its toxicologist made the chemical examination. The chemist reported the finding of morphine in the stomach. When the case came to trial the question really was not whether the accused killed his wife or not, but whether he killed her by the administration of morphine. Everything hinged upon the reliability and certainty of the tests employed by the chemist. This case resulted in a split jury and the accused husband was never tried again.

In still another case only the stomach was removed for examination. Some two years elapsed between the death and the trial. On the trial, evidence was introduced tending to show that the vomiting from which the woman suffered during the last days of her life was due to an extrauterine pregnancy. Inasmuch as the pelvic organs were not examined at the time of the obduction, this evidence could not be refuted, and again the case resulted in a mistrial.

In yet another case the stomach only was examined, two chemists failed to find any poison in the stomach. The prosecutor had a fixed idea that the man died from morphine poisoning and with the last remnant of the stomach he went to a chemist who thought that he found morphine. The case was tried and the wife of the dead man was convicted of murdering him. Later a new trial was ordered, and this time the body was exhumed and careful and thorough obduction made, and it was found that the skull had been fractured with an iron crow-bar. The wife had employed a negro to strike down her husband as he entered his home at night. Morally the woman was guilty, but the immediate cause of his death was someone else, and it was not a case of morphine poisoning.

In the legal investigation of the cause of death the medical man should make at the time accurate notes of everything he does and sees that may have a bearing upon the case. This should be done in the inspection of the body, while making the autopsy, and by the chemist, microscopist, or any scientific or medical man connected with the case. This record is known as the protocol, and this must be strictly a record of fact and absolutely without any statements of opinion. Indeed, it must be free from expressions of opinion. After the protocol has been finished the man who has made it may draw his conclusions from it, and these he may commit to writing, but on other sheets of paper. In my opinion both parties in the case should have copies of the protocol, but conclusions that are drawn from it are for the prosecutor alone as a rule, at least until stated by the witness on the stand. For instance, in making the obduction it would be the duty of the man making the section to note fractures of the skull, structural diseases of the heart or, in short, any abnormality, but it would be improper to state in the protocol that death resulted from this or that condition. It is proper for the chemist to state in his protocol that in the contents of the stomach or in so many grams of the liver he found so much arsenic, but it would not be proper to insert that this is enough to cause death. If the mucous membrane of the stomach shows erosions, statement to this effect should be made in the protocol, but a statement of an opinion as to the cause of these erosions would not be proper. In making an inspection of the dead body, which is sometimes technically called "view," all the surroundings should be observed and should be noted. A photographer may very properly be called into service here, but if so he must photograph things as they are and no rearrangement should be permitted. The conditions under which bodies are inspected are unlimited in variety, and the object should be to get a true picture either in written words or by the camera, or by both means. The environment should be closely scrutinized, footprints, evidence of a struggle, the presence of a weapon, the existence of powders or liquids that may contain the remnants of poison, and in fact everything should be seen and when seen their exact location with reference to the body should be recorded, and in doing this it is better to make exact measurements than to guess. If the body be clothed, the color, texture, arrangement, etc., of the dress should be recorded. The position of the body and its relation to other things may be matters of great importance. In one case in my experience it was found to be quite pertinent to determine whether the victim had vomited before or after he fell, and so slight a thing as a string of mucus extending from the dead lips to the vomited matter on the floor played quite a role in determining the truth of the story of the man who first reported

the murder and was finally convicted of the crime. The position of the hands of the deceased, are they closed, do they grasp anything, do they bear any marks of a struggle, are there stains on the face, hands or clothing of the deceased. All this and more must not be overlooked. Especially when the victim is a woman and attempted rape may have led to the murder, the underclothing should be carefully examined and seminal stains and bruises of the external genitals may be found. If there be wounds they should be carefully examined and their nature determined and recorded. The presence of letters or papers about the body or in the pockets should not be overlooked, and all such articles found should be turned over to the representative of the state. The question of identity is seldom a difficult one, but when not ascertained every mark that may bear on identification should be observed and recorded. The height should be accurately determined, the weight approximated, the color of the hair, beard and eyes noted. The absence of teeth or the presence of dental plates and fillings may be of service. When the face is badly disfigured by wounds an intimate friend may fail to identify a corpse either by direct inspection or by means of a photograph. In such cases, after the face has been photographed as found, the wounds may be stitched and the face brought as nearly as possible to its natural appearance and then photographed again. The presence or absence of rigor mortis, the state of preservation or anything else bearing upon the length of time that has elapsed since death are to be noted. After the body has been closely inspected in the exact position in which it has been found, it should be stripped of clothing and placed on a hard table or board and the entire surface including the openings into all cavities carefully examined. All marks, scars, wounds, and discolorations should be carefully scrutinized and proper notes made. Possible fractures and dislocations should not be overlooked, and any discolorations or excoriations about the neck deserve careful examination.

An obduction is an autopsy made for the purpose of determining the cause of death in the case of judicial inquiry. It differs from an ordinary autopsy, which applies to section of a body, known, or at least supposed to have died from known causes, in its purpose and may differ in the details with which it is carried out. An autopsy is usually for the purpose of determining the correctness of a diagnosis. As a rule, it is chiefly concerned in the examination of certain organs. It is usually made under the belief that a certain condition will be found. In other words, an autopsy is made for the purpose of confirming what is already more or less satisfactorily known to be the cause of death, or for the purpose of adding to our knowledge concerning the pathogenic changes that occur in the disease that caused death. On the other hand, an obduction is performed upon a body the cause of death of which is as a rule unknown. Moreover, and this is of great importance, the life of another may be directly dependable upon what is ascertained in the obduction. At least two medical men are needed to make an obduction. Both should be legally qualified and neither should have any personal interest in the case. They should be authorized to do the work by proper legal authority, and under such authorization they become for the time being officials legally qualified for the work in hand. It is not my purpose to give detailed direction for making an obduction, because the medical man who needs these directions should not be trusted with a procedure which is likely to

lead to criminal prosecution. It should be borne in mind by every man who is called upon to do this work that his record becomes an official document, that it will be criticised by men who are fighting for the life of a client, and nothing short of honest, thoroughly scientific procedure on his part will stand the test. It is no uncommon occurrence to see men who have made obductions greatly humiliated in trials for murder, especially for errors of omission. Often this is due to lack of experience in the legal officer who orders a partial examination, or orders one done under conditions of time and place that render thoroughness impossible, and the same legal official when he finds his case placed in jeopardy by the incompleteness of the obduction, is quite willing that the medical man who has carried out his orders should bear the blame. A medical man should absolutely refuse to make an obduction unless the conditions are the best that can possibly be obtained. However, the conditions are sometimes such that a perfectly satisfactory obduction cannot be made. The body may not be found until decomposition is far advanced, or it may be greatly mutilated, or suspicion of homicide may not arise until months and possibly years after death, or the body may have been frozen or alternately frozen and thawed several times, or, and this happens frequently, the obduction may not be held until after the undertaker has pumped the cavities and possibly the blood vessels as well, full of some fluid. For such conditions the legal official is not responsible and the medical man will have to do, as he is compelled to do in many other instances, the best he can and take whatever criticism may come. When possible the obduction should be held within forty-eight hours after death. If possible it should be done by daylight and in private. It should be complete. The calvarium should be removed, the thoracic and abdominal cavities opened by an incision extending from the chin to the pubes. All the cavities should be opened and the organs inspected *in situ* before any of them are removed. In dissecting the scalp, injuries to the skull should be sought. After the removal of the calvarium the meninges and then the surface of the brain, so far as it can be seen, should be examined. After all the organs have been examined *in situ* the brain should be turned out and every portion of the surface examined and then this organ should be dissected, careful search for hemorrhage being made. The dissected brain should be placed in a proper receptacle and preserved for chemical examination and microscopical study. After the pleural and thoracic cavities have been examined and ligatures passed about the larger vessels, the heart should be removed, the cavities opened, the valves examined and the organ placed in a proper receptacle. If there be any suspicion of pathological change in the lung a portion should be removed for closer study and microscopical examination. The stomach with proper ligatures around the esophagus and duodenum should be separated, lifted out and opened over a clean receptacle. After careful inspection of every part of the stomach, it and its contents should be placed in a jar. The small intestine should be removed and the whole length of the intestine examined both outside and inside. The small intestine should be preserved. The liver, kidneys, pancreas and spleen should be examined and portions of each preserved in separate jars. It is best to remove and preserve both kidneys. With females the whole internal genitalia should be removed, examined and preserved. In no case should two organs or portions of two be placed in the same receptacle.

It should never be forgotten in holding an obduction that the object is not only to find the cause of death; but to exclude every other possible cause. Failure to recognize this has led to the miscarriage of many a case of trial for homicide. The prosecutor learns that Mr. Blank is suspected of having poisoned his wife who died a week ago. He investigates and finally orders the body disinterred; the stomach only is removed and sent to a toxicologist. Arsenic is found and Blank is arrested and months later the trial is on. Now, the prosecutor learns that a positive diagnosis of arsenic poisoning cannot be made from the symptoms, that Mrs. Blank suffered for years from a combination of uterine and kidney diseases, that frequently she suffered from profuse vomiting followed by collapse and that many times it was thought that she would die; that her kidneys undoubtedly were destroyed by disease, and that her ovaries had been masses of corruption for years, and the small amount of arsenic found by the toxicologist was due to the bismuth subnitrate, untold quantities of which this woman had swallowed. The prosecutor, thoroughly convinced of the guilt of the accused, feels that the case is slipping through his hands because someone has blundered, and wreaks his vengeance on the poor medical man who made the obduction and did not have sense enough to look after the kidneys and ovaries. Honest, if not learned, experts testify that every symptom that Mrs. Blank is said to have exhibited may have been due to chronic ovarian irritation combined with Bright's disease. A reasonable doubt arises in the mind of some juror and there is a disagreement. The trial has cost the county thousands of dollars and there is much grumbling among the taxpayers. Possibly the prosecutor is encouraged, persuades the board of supervisors to employ eminent legal help and the case is tried again, but most likely the same result follows. This is not an overdrawn statement, and its actual occurrence is not infrequent in the annals of criminal law. Much time and labor have been lost; much money has been expended and justice has wholly miscarried simply because the obduction was not properly conducted.

Concerning the organs to be submitted to the toxicologist, there are two widely adopted customs that should be abolished because they frequently lead to perplexities the solution of which may be well nigh impossible. First, it is generally assumed that in suspected poisoning the stomach only, or at most the stomach and the duodenum, is needed by the chemist. The chemist needs, in addition to the stomach and duodenum, a portion of the liver, one kidney, the urine if there be any in the bladder at the time of the obduction, the heart or half of this organ and a portion of the brain. In exceptional instances he may need portions of other tissues, but those mentioned above should be furnished him in every case. Each organ or part should be placed in a jar by itself. That this advice is important the following statement of the happenings in a case may be mentioned:

The stomach and rectum were placed in one jar and in these tissues together the chemist found an amount of arsenic which he estimated for the entire content of the jar to be as much as 20 grains, but he could not say how it should be apportioned to the organs. All the arsenic might have been, when the tissues were removed from the body, in the one or in the other. The defense claimed that a large amount of white arsenic had been suspended in water and injected

into the rectum a few hours after death. It will be seen from this that the advice to place each organ or part in a receptacle of its own is not due to a whim, but is founded upon practical experience.

The use of some preservative for the tissue removed for examination is sometimes necessary. Fortunately within recent years formaldehyde has become the basis of embalming fluids, the best of which consists of an 8 to 10 per cent solution of this substance with from 2 to 5 per cent of potassium nitrate. These are the essential ingredients of Kaiserling's solution and for both the toxicologist and the pathologist this can hardly be improved. When the body has been well embalmed with the above mentioned fluid, the addition of a preservative to the removed organs is not necessary. If too dry a small quantity of embalming fluid may be added.

The second mistake, which is well nigh universally practiced and which should be continued no longer, is founded upon the theory that in cases of suspected poisoning a chemical examination only is desirable. In every case of suspected poisoning, portions of the walls of the stomach, liver, kidney, heart and brain, and in the female, of the ovaries and uterus should be properly hardened, sectioned, examined microscopically and preserved as exhibits. The proper carrying out of these procedures would prevent many complications and positively dispose of many doubts that arise in trials for murder by the administration of poison. As has been stated a frequent defense in these cases is that the deceased came to his death from natural causes and this claim would be easily disposed of if microscopical preparations from the organs above mentioned were made. Moreover, the object of the prosecutor is not to convict; it is to see that justice is done and this can be secured with certainty only after a most exhaustive search for the cause of death. Some poisons induce highly characteristic histological changes and the finding of these would furnish valuable confirmatory evidence in case the presence of the poison is obvious by chemical tests. Again, the deceased may have had a diseased heart, liver, kidney, or other organ, and yet death may have been due to the administration of poison. In such instance it would certainly be well for the prosecutor to know the facts. Not only is the histological examination of tissues neglected in cases of suspected murder by the administration of poison, but in many such cases the gross examination of all the parts of the body is neglected. This is a way of opening up a sure and safe escape for the accused.

The expert in examining into a gunshot injury should be alert, and carefully observe all the surroundings at the place where the wound was inflicted. Photographs are desirable and their veracity cannot be questioned. The position of the body of the wounded man at the time he received the shot should be determined. His clothes should be examined for holes, burnt spots and stains. The position of the assailant may in some cases be determined quite positively or facts that show that the accused's account of the injury cannot possibly be true may be brought to light; or on the other hand the accused's claim may be substantiated.

There is no law and apparently no common custom governing the transfer of portions of the body or other material, suspected to contain poison criminally introduced, to the toxicologist.

A chemist who has done much toxicological work could keep busy and get himself into all kinds of trouble if he would listen to all the requests made to him. He receives frequent letters from persons in many walks of life, telling of suspicions of attempted poisoning and asking him to make analyses. A wife suspects that her husband has put some deadly drug in her food; she wants her suspicion kept profoundly secret. She would not hint it to anyone, but she would be under many obligations to the chemist if he would make an analysis and set her mind at rest. Other requests are more authoritative: A physician thinks someone, usually husband or wife, is administering poison to his patient by putting it in his medicine. There is only one proper answer to make to all these requests whatever their source and it is this: "If you suspect that someone is using or attempting to use poison in a criminal way, report your suspicion to the prosecutor of your county and deliver any suspected material you may have into his hands. I can have nothing to do with any suspected material unless I receive it through official channels." It is the duty of the prosecuting attorney to inquire into the commission of crime and the toxicologist had better leave these matters to the official.

Usually the material for toxicological examination placed in clean fruit jars, only one organ or part of organ in one jar, is sealed by the official in charge of the case, prosecutor or assistant, sheriff or assistant, or by the medical men who have made the autopsy, and carried or sent by express to the toxicologist. Any of these methods of transmission seem to be satisfactory to the courts providing the material can be traced and the possessor at every stage identified. Usually in the course of the trial the medical man who made the obduction testifies that he removed such organs and placed them in jars, which to his knowledge must have been free from poison, sealed them (describing the seal) and delivered them to some official (prosecutor or sheriff usually or an assistant to one of these). Then the official testifies that he received them (seals unbroken) and transferred them to the toxicologist either in person or through the express company.

A protest should be made against the usual method of sealing jars containing material for the toxicologist. Fruit jars are suitable and are usually selected and the cap is covered with a mass of sealing wax. This is crude, not distinctive and is removed with difficulty. After the material is placed in the jar, the cap should be screwed on and the whole jar should be wrapped in heavy paper after which a tape string should be passed around the jar both longitudinally and horizontally. The distinctive seal should be placed on the points where the longitudinal and horizontal tapes and strings cross.

When the chemist receives the material directly from an official or his representative he should give a receipt in which he should specify the number and kind of jars and any labels that they may carry. He should not say in this receipt "I have this day at 10 A. M., received from John Jones, Sheriff of Ralls County, the stomach of Jane Potter," but he might say "I have this day at 10 A. M., received from John Jones, Sheriff of Ralls County, a quart Mason fruit jar said to contain the stomach of Jane Potter." On receipt of tissue for toxicological examination the chemist should place the material under seal and so keep it that he can testify that no one, save himself, has had access to it and

when the trial is on he should be able to produce all receptacles in which the organs were brought to him with such parts that have not been destroyed in making the chemical analysis. The toxicologist should keep a seal on his lips as well as on his private work room or his poison case. Troublesome inquiries should be referred to the attorney in charge of the case and this is usually the prosecutor; however, there are instances in which toxicological work is done for the defense, and very rarely the trial judge orders an examination made by independent parties for himself. We have known of this having been done in one instance and after receiving the report of the toxicologist the trial judge dismissed the case, although the chemist employed by the prosecution had reported the presence of a poison. This case was not brought to a hearing before a superior court and there is, so far as we know, no ruling on this point.

The question of the amount of poison recovered by the chemist from the tissue is a constantly recurring one in trials for homicide by this means. The courts of all civilized countries have generally held that it is not necessary for the chemist to show that there is a fatal dose in any organ or even in the whole cadaver. If poison be found and the jury be convinced that the accused administered it, this is generally held to be sufficient to convict. Homicide by the administration of poison is always premeditated murder. This of course does not include accidental poisoning in which a poisonous substance is administered by mistake when something else was intended. If it can be shown that John Jones administered a poison to his wife knowing or believing that it was a poison, it is assumed that he gave it with ill intent. He cannot claim, for instance, that he was giving her arsenic as a tonic or to improve her complexion and that she died from some other cause and that the arsenic found in her body by the chemist is thus accounted for.

If the chemist can isolate the poison sufficiently pure to determine the amount this should be done. Moreover, he should if possible preserve portions of the poison and visible tests, to serve as exhibits. This can usually be done with the inorganic poisons, but exhibits of the poison cannot be demanded with many of the more deadly organic poisons. Rarely crystals of strychnin, morphin, chloral and other organic poisons can be obtained not only in quantity sufficient for all the necessary test, but some may remain for exhibits.

—*V. C. V.*